ROLE OF SERUM ALBUMIN AS A PROGNOSTIC MARKER OF OUTCOME IN PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY

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Dedicated

to

my Family

&

Teachers

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Dr.VikramChaudhary

ABBREVIATIONS

APACHE	Acute Physiology and Chronic Health Evaluation
ATP	Adenosine Triphosphate
BBB	Blood Brain Barrier
CT	Computerised Tomography
CSF	Crebrospinal Fluid
COP	Colloidal Osmotic Pressure
DALY	Disability Adjusted Life Years
Da	Dalton
dl	Decilitre
EDH	Extra Dural Haemorrhage
EPC	Endothelia Progenitor Cell
FDR	Fractional Degeneration Rate
GCS	Glasgow Coma Rate
g	Grams
g/d	Gram per Day
GTP	Guanosinetriphosphate
GFAP	Glial Fibrillary Acidic Protein
GOS	Glasgow Outcome Score
HSP	Heat Shock Protein
ICU	Intensive Care Unit
ICP	Intracranial Pressure
IL	Interleukin
i.v	Intravenous

Kda	Kilo Dalton
Kg	Kilogram
LCFA	Light Chain Fatty Acid
LDH	Lactate Dehydrogenase
MRI	Magnetic Resonance Imaging
MBP	Myelin Basic Protein
M RNA	Messenger Ribonucleic acid
MMP	Matrix metalloproteinase
Ml	Millilitre
NO	Nitric Oxide
NDMA	N- methyl D- aspartate
NSE	Neuron Specific Enolase
NF_H	Neurofillament- H
O2	Oxygen
OR	Odds Ratio
PT	Prothrombin
RTI	Road Traffic Incidence
SDH	Subdural Haemorrhage
TBI	Traumatic Brain Injury
T RNA	transcription Ribonucleic Acid
UCH	Ubiquitin Carboxyl-terminal Hydroxylase
WBC	White Blood Cell

KEY TO MASTER CHART

C	Conservative
DAI	Diffuse Axonal Injury
F	Favourable
Fe	Female
GOS	Glasgow Outcome Score
g/dl	Grams per Decilitre
gm/dl	Grams per Decilitre
Hypo	Hypoalbuinemia
M	Male
N	No
Normal	Normal albumin
NS	Non Survival
Per	Percentage
RSA	Road Side Accident
TSP	Total Serum Protein
S	Survival
Su	Surgical
SD	Standard Deviation
S ALB D1	Serum Albumin Day 1
S ALB D3	Serum Albumin Day 3
S ALB D7	Serum Albumin Day 7
S ALB D10	Serum Albumin Day 10
UF	Unfavourable
Y	Yes

ABSTRACT

INTRODUCTION: Traumatic brain injury still remains a serious concern and one of the leading causes of death and disability, particularly among young adults. Very few biomarkers of the severity of head injury are clinically available.

AIM: To study the role of serum albumin as a marker for predicting prognosis in patients admitted with severe head injury Glasgow coma score of less than and equal to 8.

MATERIAL AND METHODS: This study is a prospective study conducted in department of Neurosurgery, Dayanand Medical college and Hospital from February 2018 to July 2019. Total 110 patients with severe traumatic brain injury which qualified the inclusion and exclusion criteria were studied. On admission the serum albumin of the patient was noted, appropriate management plan was decided based on examination and CT findings. Patient underwent serial assessment of their serum albumin at the day 1 (on admission), day 3, day 7 and day 10 of the stay. The outcome of the patient was assessed according to Glasgow outcome score at the time of discharge.The mean value of serum albumin was correlated to the outcome of the patients at discharge, duration of stay in hospital, duration of ventilator support required, and complications.

RESULTS: Age, gender, mode of injury and diagnosis had no impact on outcome. Mean serum albumin on admission was significantly higher in group with favorable outcome as compared to group with unfavorable outcome. Percentage fall in serum albumin in unfavorable group at day 3, day7, day10 was significantly higher than favorable group. Mean serum albumin level on admission of survival group was 3.47±0.09 g/dl and that of non survival group was 3.37±0.08 g/dl.The percentage fall of serum albumin was significantly higher in non survival. Patients with low serum albumin on admission had longer hospital stay, ICU stay and more ventilator support requirement. Rate of complication was significantly higher in hypoalbuminemiagroup, as compared to patients with normal serum albumin had complications.

CONCLUSION: Serum albumin estimation in severe traumatic brain injury can be used as prognostic marker of outcome.

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INTRODUCTION

Traumatic brain injury still remains a serious concern and one of the leading causes of death and disability, particularly among young adults.[1] The uncertainty that exists about the likely outcome after traumatic brain injury (TBI) is encapsulated in the Hippocratic aphorism: “No head injury is so serious that it should be despaired of nor so trivial that it can be ignored.” Today, physicians’ estimates of prognosis are still often unduly optimistic, unnecessarily pessimistic, or inappropriately ambiguous.[2] It still remains impossible to say with certainty what will be the future course of events in an individual patient, but intensive research in the last two decades has made it possible to be much more confident about what is likely to happen, and to consider prognosis in terms of probabilities rather than prophecies.[3] TBI is a significant public health problem worldwide and is predicted to surpass many diseases as a major cause of death and disability by the year 2020. There is some data to indicate that the majority of TBI cases (60%) are as a result of Road traffic incidents(RTI), followed by falls (20-30%), and violence (10%). In addition to being a major cause of mortality, injuries are also associated with increased disability and morbidity. According to the World Health Organization, the Disability Adjusted Life Years (DALYs) losses are higher for low-income countries due to injuries for nearly all causes and Traumatic Brain Injury (TBI) is an important and often critical sequel of these injuries.[4]

In Asian countries the rapid urbanization has increased the risk of TBI.[5] India remains in the leading position in the world in fatalities due to road accidents.[4] Even if people survive, the concomitant physical disabilities, long-term cognitive and psychological damage pose a major threat. With the subsequent secondary damage setting insidiously, the pathological sequel warrant a multidisciplinary approach for management and longer period of stay in the ICU setting. It takes a heavy toll on both financial status of the patients and the hospital’s available resources. In order to mitigate the misery of the patients and to judiciously allocate the hospital

resources, it becomes mandate to predict the favorable outcome earlier in order to take decision whether to continue aggressive therapeutic measures or not.[6]

Traumatic brain injury can be classified into two types, primary and secondary. The primary injury occurs at the time of the accident causing direct damage to nerve tissue. Secondary damage is not seen at an early stage, but is the natural and physiological response to the initial injury. Early determination of prognosis after traumatic brain injury is a priority for relatives and physicians involved in the care of these patients. New prognostic information beyond the clinical examination, patient demographics and radiological imaging from admission is needed to allow early prediction of short, mid, and long term outcome of patients with moderate and severe traumatic brain injury.[7]

Prediction of outcome involves making probability statements that depend on a logical relationship between outcome and features encapsulated in antecedent, early data. The advances in prognosis reflect the establishment of methods for categorizing outcome[8] and early injury severity.[9] Although clinicians usually attempt to take a wide range of factors into account when making clinical decisions and assessing prognosis, there is probably a redundancy in this effort to be complete. In practice, relatively few features have been found to contain most of the prognostic information,[3] These include the patient age, clinical indices indicating the severity of brain injury (e.g., the depth and duration of coma and other neurological abnormalities), and the results of investigation and imaging studies, particularly intracranial pressure (ICP) and computed tomography (CT) scanning, which disclose the nature of brain injury and its effects on intracranial dynamics. Even though there is little doubt regarding the importance of these features from clinical experience, there are still debates about the precise nature of their relationships and about exactly how the different features should be assessed, categorized, and—most importantly-utilized.[3]

Traumatic brain injury (TBI) is a heterogeneous disorder characterized by acute brain injury resulting from external mechanical forces exerted on the head. In clinical settings, the Glasgow Coma Scale (GCS) is commonly used to stratify the severity of TBI, where mild TBI (mTBI), moderate TBI and severe (sTBI) constitute a GCS score of 13-15, 9-12 and 3-8 respectively.[10]

Assessment of TBI

There are different systems available to evaluate the extent of brain injury. Neuro-psychological examination like Glasgow Coma Scale (GCS) and pupil response are widely used for the assessment of the severity of brain injury.[11] The neuroimaging techniques, such as computed tomographic scanning (CT scan) and magnetic resonance imaging (MRI) have emerged as the choice of investigation. But all these have limitations such as poor sensitivity and failure to detect secondary pathological events.[12] Hence exhaustive research has been carried out for identifying better prognostic marker, preferably a serum bio marker. These efforts to identify an ideal biomarker which could reflect the pathology of TBI and secondary injury have yielded meager success. This is evident from the finding that the markers released from the brain cells are also elevated in non- brain pathological conditions and are non-specific.[13]

Behavior	Response	Score
Eye Opening Response		
	Spontaneously	4
	To speech	3
	To pain	2
	No response	1
Best Verbal Response		
	Oriented to time, place, and person	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No response	1

Best Motor Response

Obeys commands	6
Moves to localized pain	5
Flexion withdrawal from pain	4
Abnormal flexion (decorticate)	3
Abnormal extension (decerebrate)	2
No response	1

Total Score: 15

Comatose: 8 points or less

Totally unresponsive: 3 points

Mild brain injury = 13-15 points;

Moderate Brain Injury = 9-12 points;

Severe Brain Injury = 3-8 points

The neurobiological changes following TBI are complex and not fully understood. Some layers of complexity arise from unique anatomical features such as the elongated shape of a neuron, the skull that both protects the brain and constitutes a harmful closed compartment in the case of intracranial volume expansion, the cerebrospinal fluid and blood-brain barrier (BBB), which both maintain and perpetuate the unique intracerebral environment.

The BBB is highly selective and plays an important role in allowing proteins or biomarkers entering the blood stream. In the acute phase of TBI, the disruption of the BBB may cause vasogenic or cytotoxic brain edema, leading to the expansion of brain volume, which in turn increases intracranial pressure (ICP), impairs cerebral perfusion and subsequently causes ischemic injury.[10]

Structural injuries to the brain can be categorized into focal and diffuse. Focal injuries are usually associated with higher energy trauma and include cortical or subcortical contusions and lacerations as well as intra cerebral haemorrhage.[10]

In the brain, local and systemic inflammation work in concert to contribute to secondary brain injury, the cerebral analog to the systemic inflammatory response/compensatory anti-inflammatory response phenomenon

described peripherally. The protection or “immunologic privilege” the brain usually enjoys is disrupted in moderate-to-severe TBI.[7]

In the absence of the relative fortification of the blood-brain barrier (BBB), a bidirectional flow of inflammatory mediators transits between the systemic circulation and the brain. The brain is both a target and an effector organ, as glial cells and neurons both produce immunologic mediators (i.e., complement, acute phase proteins, and cytokines) and exhibit receptors for these substances. This interchange produces local tissue damage and a systemic response.[14]

The initial moments after a traumatic injury can be categorized in two concurrent phases as follows: metabolic crisis and excitotoxicity. In response to direct tissue injury, the cerebral metabolism is deranged, leading to the accumulation of lactic acid due to anaerobic glycolysis, increased membrane permeability, and edema formation. Autoregulation of cerebral blood flow is impaired, promoting energy failure. In parallel, there is massive release of excitatory neurotransmitters, resulting in oxidative damage. The consequence of these processes is membrane degradation and BBB compromise. Membrane degradation fosters unregulated transit of immune molecules in and out of the injured brain. BBB breakdown is present even in diffuse injury.[15]

Traumatic brain injury (TBI) also affects functioning of various organ systems in the absence of concomitant non-neurologic organ injury or systemic infection. After the initial trauma, a second phase of brain injury begins. Secondary brain injury results from a complex sequence of events that begins just after the initial insult and continues through the acute hospitalization. Mitigating secondary brain injury represents a key target in the fight to limit disability incurred from TBI. Secondary brain injury results from a diverse host of etiologies, including (but not limited to) edema, ischemia, excitotoxicity, and inflammation. Excitotoxicity occurs when a neuron is destructively stimulated with excess amounts of neurotransmitter, especially glutamate. In experimental conditions,

inflammation is increasingly recognized to be an important source of secondary brain injury. In the clinical setting, however, inflammation's contribution to secondary TBI is less well established. The systemic manifestations of TBI can be mild or severe and can present in the acute phase or during the recovery phase. Non-neurologic organ dysfunction can manifest following mild TBI or severe TBI.[16,17] The pathophysiology of systemic manifestations following TBI is multifactorial and involves an effect on the autonomic nervous system, involvement of the hypothalamic-pituitary axis, release of inflammatory mediators, and treatment modalities used for TBI. Endocrine dysfunction, electrolyte imbalance, and respiratory manifestations are common following TBI. The influence of TBI on systemic immune response, coagulation cascade, cardiovascular system, gastrointestinal system, and other systems is becoming more evident through animal studies and clinical trials. Systemic manifestations can independently act as risk factors for mortality and morbidity following TBI. Some conditions like neurogenic pulmonary edema and disseminated intravascular coagulation can adversely affect the outcome.

Trauma, with or without TBI, results in a dysregulation of the immune system, predisposing patients to nosocomial infections and worse outcomes. Investigators are just beginning to appreciate immunologic dysfunction or dissonance as a source of worsening neurologic injury. Clinical evidence in humans has lagged behind the observations made in animal models. Advances in technology allow markers of inflammation such as cytokines and chemokines to be measured in the clinical setting, providing an emerging body of clinical research.[18,19]

Improvements in biochemistry and molecular biology have lead to a greater understanding of the process that follows traumatic brain injury. In particular, the role of inflammatory mediators in the development of secondary brain injury has been extensively investigated. A variety of mediators are implicated including cytokines, free radicals, amino acids and nitric oxide. Current research has focused on the expression of these

cytokine responses in animal and human studies and has allowed insight into the mechanisms of primary and secondary brain injury, particularly the resultant effects on cellular metabolism and microvascular blood flow. Subsequently, further research has focused on whether modulating the inflammatory response may improve neurological outcome. Amongst the cytokines interest has particularly focused on interleukin 1b (IL-1b), tumour necrosis factor a (TNFa) and interleukin 6 (IL-6). Early after injury astrocytes and microglia release IL-1b and TNFa leading to further cytokine release and production of mediators from the peripheral immune system. Toxic effects can be demonstrated in laboratory studies and clinical studies have demonstrated increased levels of TNFa in patients with TBI. The role of IL-6 is more ambiguous as it has both pro- and anti-inflammatory actions .IL-6 levels in plasma and CSF are increased after both neurosurgery and TBI .Free radicals are highly reactive compounds such as superoxide (O2 −) and nitric oxide (NO). They damage endothelial cells and contribute to vasogenic and cytotoxic oedema. Nitric oxide and endothelin have also been implicated in the patterns of abnormal cerebral blood flow following TBI. These include initial cerebral oligaemia in the first 48–72 h and hyperaemic and vasospastic phases at 72 h and 5–7 days respectively. The expression of these cytokines may represent the cellular manifestations of failing autoregulatory mechanisms. Excitatory amino acids, in particular glutamate, are released from damaged cells and stimulate a cascade of intracellular reactions that can result in cell death. Part of the process is mediated by the N-methyl-D-aspartate (NMDA) receptor, and NMDA receptor antagonists ameliorate secondary injury in animal models .The effect of manipulating the inflammatory response has been examined in a number of clinical trials. The results of trials of oxygen derived free radical scavengers, NMDA receptor antagonists and 21-aminosteroids, have been disappointing. The use of moderate hypothermia to limit the inflammatory response may offer more promise.[6]

One of the factors involved in secondary damage that may occur following head trauma is the changes in blood parameters and biomarkers. Assessment of brain damage using biochemical tests and cerebrospinal fluid (CSF) and serum enzymes during the past decade has been done. Biomarkers of structural damage such as S-100, tau, Neuron Specific Enolase (NSE) and myelin basic protein (MBP) may be used as potential diagnostic tools, prognostic and therapeutic supplements. Clinical and laboratory research in the past two decades had shown that all neurological damage does not occur at the moment of impact but evolves over the ensuing hours and days, with the primary injury initiating a secondary injury cascade, leading to deleterious pathophysiological and biochemical reactions. Surprisingly, only a few biochemical markers have been identified to prognosticate the severity of trauma at the tissue level[20,21,22]

The acute inflammatory response, designed to be protective mechanisms, can override at times, leading to unfavorable outcome. Considerable attention has been directed towards the utility of acute phase reactants as prognostic marker for predicting outcome. Among the acute phase reactants albumin is ideally a candidate for research as the measurement is easily available and routinely done.[23]

Albumin (69Kda) is the major protein of the human plasma accounting to about 60% of the total plasma protein.[11] Albumin is produced by the liver at a rate of 9 to 12 g/day. Its hepatic synthesis is primarily affected by osmotic colloid pressure and inflammatory states, but also, and to a lesser degree, by nutritional status and hormones. It is one of the negative acute phase reactants and its level tend to fall in the plasma as a result of injury or infection independent of the nutritional status.[24] Many studies had highlighted the role of albumin as a prognostic marker in life threatening illnesses, various types of cancer such as colorectal, lung and breast cancer.[23] It has also been studied to determine the clinical outcome following cardiac surgery.[25] Du Chen, Long Ba, et al, have studied the

use of serum albumin along with pre-albumin to predict the poor outcome in TBI and observed serum albumin serve as a better marker.[26]

Serum albumin is a widely used method of accessing nutritional and inflammation status in both acute and chronically ill patients. Al-though many studies explored the relationship between serum albumin levels and the duration of weaning in patients with mechanical ventilation, but its effect on patients' outcome of weaning was still unknown.[27]

Acute disease, injury or infection are associated with a decline in the serum albumin levels. Major physiologic stress causes the release of hormones which alter the metabolic rate and mobilize fuel sources. The liver responds to acute stress by producing mediators of acute phase response.[28] Albumin is not an acute phase reactant, so it's synthesis may diminish. The acute phase response is mediated via the release of cytokines such as Tumour Necrosis Factor and Interleukin 1. The increased synthesis of acute phase proteins and the synthesis of albumin is reciprocally related at the transcriptional level.[29] Thus, increased production of acute phase reactants causes reciprocal decrease in the serum albumin levels. This decrease in serum albumin levels is further compounded by a shift in the distribution of albumin from the intravascular compartment to the interstitial compartment. Excessive degradation of albumin during stress adds further to the decreased albumin levels.[30]

Of the above mentioned causes, it has been found that the major cause of hypoalbuminemia in systemic injury is increased vascular permeability and not necessarily due to malnutrition, elevation of cytokines such as interleukin-1(IL-1), tumour necrosis factor (TNF-α) and interleukin-6 (IL-6). Other mechanisms proposed include haemodilution, decreased synthesis and increased protein catabolism. Though serum albumin levels are known to fall in the first few days following head injury, hypoalbuminemia at admission has, so far, not been studied in detail.[31] A few studies have demonstrated hypoalbuminemia in mild, moderate and severe head injury at admission. Mean admission serum albumin level, in these studies,

showed a positive correlation with GCS at admission, as the elevation of IL-6 likely corresponds with the increasing severity of injury. Many studies have suggested serum albumin to be a valuable prognostic indicator in critically ill patients and not necessarily a marker of only nutritional status.[32] Studies show a significant association of admission hypoalbuminemia with unfavorable outcome at 3 months, following head injury. Though being found more in severe head injury as compared to mild or moderate injury, hypoalbuminemia was noted in multivariate analysis to be definitely associated with unfavorable outcome, independent of the influence of admission GCS. Among patients of similar GCS, those with hypoalbuminemia at admission fared poorly compared to those with normo-albuminemia. Considering the fact that very few biomarkers of the severity of head injury are clinically available, it is imperative to study each in relation to neurological outcome.[33]

AIMS & OBJECTIVES

To study the role of serum albumin as a marker for predicting prognosis in patients admitted with severe head injury defined as having Glasgow coma score of less than and equal to 8.

REWIEW OF LITERATURE

Severe Traumatic Brain Injury (TBI) is a major cause of disability and death in the young. Severe TBI initiates a complex cascade of metabolic perturbations with the primary injury triggering secondary events that evolve over many days, leading to deleterious pathophysiological and biochemical reactions. Numerous studies have consistently demonstrated increased protein catabolism following TBI. Surprisingly, only a few biochemical markers have been identified to prognosticate the patients' response to brain injury. These markers also exhibit changes over time in patients of trauma as a component of metabolic response to injury or infection (MRII), independent of the nutritional status.[34]

Albumin was one of the first human proteins to be isolated and extracted from plasma for clinical use. First crystallized in 1934, a preparation was made available for clinical use in the 1940s [35,36]. Early successful use in multi-trauma and severely burned patients led to rapid expansion of the so-called human albumin program in the USA [37], and albumin use spread from the military setting to civilian hospitals and into regular use in operating and emergency rooms around the world. The first commercially available preparations of intravenous human albumin solution were developed using the cold alcohol fractionation technique created by Edwin Joseph Cohn [35,37]. Later developments and refinements in extraction and processing have resulted in increasingly pure solutions.[38]

The function of circulating albumin in critical illness is not fully understood. It may differ significantly from that in healthy subjects. A low serum albumin concentration in critical illness is associated with a poor outcome.[39,40]

In humans, albumin is the most abundant plasma protein, accounting for 55–60% of the measured serum protein. It consists of a single polypeptide chain of 585 amino acids with a molecular weight of 66 500 Da. The chain is characterized by having no carbohydrate moiety, a scarcity of tryptophan and methionine residues, and an abundance of charged

residues, such as lysine, arginine, glutamic acid and aspartic acid. The mature, circulating molecule is arranged in a series of α-helices, folded and held by 17 disulphide bridges. The folding creates subdomains of three contiguous α-helices in parallel.[41,42] A pair of subdomains face each other to form domains. These can be seen as cylindrical structures with polar outer walls and a hydrophobic central core.[43]

The tertiary structure of human albumin crystal has been isolated by x-ray crystallography. It is seen as a heart-shaped molecule 80 × 30 Å.36 In solution, the shape is quite different. The three domains appear to be arranged in an ellipsoid pattern, giving the molecule low viscosity . [43,44]

The serum albumin concentration is a function of its rates of synthesis and degradation and its distribution between the intravascular and extravascular compartments. The total body albumin pool measures about 3.5–5.0 g kg^{-1} body weight (250–300 g for a healthy 70 kg adult). The plasma compartment holds about 42% of this pool, the rest being in extravascular compartments. Some of this is tissue-bound and is therefore unavailable to the circulation. Each day, 120–145 g of albumin is lost into the extravascular space.[45,46] Most of this is recovered back into the circulation by lymphatic drainage. Albumin is also lost into the intestinal tract (about 1 g each day), where digestion releases amino acids and peptides, which are reabsorbed. There is minimal urinary loss of albumin in healthy subjects. Of the 70 kg of albumin that passes through the kidneys each day, only a few grams pass through the glomerular membrane. Nearly all of this is reabsorbed, and urinary loss is usually no more than 10–20 mg day^{-1}.[47]

The distribution of albumin between body compartments can be examined by injecting radiolabelled albumin into the venous circulation. A typical biexponential plot of log plasma concentration versus time shows a first-order process . A two-compartment model can be constructed. There is a rapid phase of disappearance from the plasma over the first 2 days. This represents the transcapillary exchange rate of 4.5% h^{-1}, giving a

distribution half-time of about 15 h. Then there is a slower exponential decay, representing the fractional degradation rate (FDR), of about 3.7% day^{-1} with an elimination half time of about 19 days. The FDR closely parallels the rate of synthesis in steady state (3.8% day^{-1}).[47]

The mechanism of the escape of albumin into the extravascular compartment has come under review recently. Albumin must cross capillaries. Most organs in the body have continuous capillaries, but in some there are wide-open sinusoids (liver, bone marrow) or fenestrated capillaries (small intestine, pancreas, adrenal glands). Starling's theory holds that the rate of escape depends on the permeability of the wall and hydrostatic and oncotic pressures on either side of the wall. Half of the escaping albumin does so through the continuous capillaries, and there appears to be an active transport mechanism to facilitate this.[48,49] Albumin binds to a surface receptor called albondin, which is widely distributed in many capillary beds, except in the brain. Bound albumin enters vesicles within the endothelial cell and is discharged on the interstitial side within 15 s. The rate of transfer is increased with the addition of long-chain fatty acids (LCFAs) to albumin, and with the cationization and glycosylation of the molecule.[50]

In humans, albumin synthesis takes place only in the liver.Albumin is not stored by the liver but is secreted into the portal circulation as soon as it is manufactured. In healthy young adults, the rate of synthesis is 194 (SD 37) mg kg^{-1} day^{-1}, or about 12–25 g of albumin per day. The rate of synthesis rate varies with nutritional and disease states. The liver can increase albumin synthesis to only 2–2.7 times normal because most of the liver's synthetic machinery is already devoted to albumin at rest. The synthetic pathway is common to eukaryotes and is also used for synthesis of other proteins.[46,51,52]

Albumin will be synthesized only in a suitable nutritional, hormonal and osmotic environment. The colloid osmotic pressure (COP) of the interstitial fluid bathing the hepatocyte is the most important regulator of albumin

synthesis. Synthesis requires: mRNA for translation; an adequate supply of amino acids, activated by binding to tRNA; ribosomal machinery for assembly; energy in the form of ATP and/or GTP. The mRNA concentration available for action on ribosomes is an important factor controlling the rate of albumin synthesis. Trauma and disease processes will affect the mRNA content. A reduction in albumin mRNA concentration, caused by a decrease in gene transcription, is seen in the acute-phase reaction mediated by cytokines, mainly interleukin-6 (IL-6) and tumour necrosis factor α (TNF-α). A decrease in gene transcription is also seen in hepatoma cells and in hepatocytes damaged with carbon tetrachloride.[46,53]

The hormonal environment can affect the mRNA concentration. Insulin is required for adequate albumin synthesis. Diabetic subjects have a decreased synthetic rate, which improves with insulin infusion. Perfused livers of diabetic rats have a 50% decrease in gene transcription. Corticosteroids have complex effects on albumin synthesis. There is increased albumin synthesis with combinations of steroids and insulin, and of steroids with amino acids. Hydrocortisone and dexamethasone both increase gene transcription *in vitro*, but the overall *in vivo* effects are complex. Steroids also increase albumin catabolism. Growth hormone has been shown to stimulate gene transcription in cultured hepatocytes.[54,55]

The rate of synthesis depends on nutritional intake, more so than for other hepatic proteins76 Fasting reduces albumin production, but specifically omitting protein from the diet causes a greater reduction in synthesis. Early in protein deprivation, there is rapid disaggregation of free and bound polysomes, which can be reversed rapidly by refeeding the subject with amino acids. Two amino acids are particularly effective, tryptophan and ornithine. Ornithine, unlike tryptophan, is not incorporated into albumin. It is a product of the urea cycle and acts as a precursor of the polyamine spermine. The increases in polysome aggregation and albumin

synthesis with ornithine refeeding suggest that the urea cycle plays more of a role in protein metabolism than mere waste disposal. Protein deprivation for a longer time leads to a 50–60% decrease in the activity and concentration of the mRNA, presumably through increased breakdown, as gene transcription is not slowed in rats on a 0–4% protein diet.[56,57]

Total daily albumin degradation in a 70 kg adult is around 14 g day^{-1} or 5% of daily whole-body protein turnover. Albumin is broken down in most organs of the body. Muscle and skin break down 40–60% of a dose of labeled albumin. The liver, despite its high rate of protein metabolism, degrades 15% or less of the total. The kidneys are responsible for about 10%, while another 10% leaks through the stomach wall into the gastrointestinal tract.[56]

The mechanism of breakdown involves uptake into endocytotic vesicles, which fuse with lysosomes in endothelial cells. This may involve binding to endothelial surface membrane scavenger receptors, called gp18 and gp30, which are widespread in the body tissues. They bind altered or denatured albumin, and it is likely that chemical modification of the circulating albumin is a signal for receptor-linked lysosomal degradation.[58,59] It is also possible that modification prevents degradation. Binding of LCFAs to albumin seems to protect the molecule from breakdown. In analbuminaemia, the LCFA/albumin ratio is increased and degradation is suppressed. The final breakdown products are free amino acids that add to the pools of amino acids within cells and in the plasma.[60]

Critical illness alters the distribution of albumin between the intravascular and extravascular compartments. There are also changes in the rates of synthesis and degradation of the protein. The serum albumin concentration will decrease, often dramatically, from early in the course of a critical illness. It will not increase again until the recovery phase of the illness. The kinetics of albumin given i.v. will differ greatly between

critically ill patients and healthy subjects. The implication of this, given the important functions albumin has in health, is that using exogenous albumin to increase the intravascular albumin concentration during critical illness is beneficial. But studies have failed to show any benefit of albumin over other colloidal therapies in adults.[61,62]

The altered distribution in critical illness is related to an increase in capillary leakage. This occurs in sepsis and after major surgical stress. It involves dysfunction of the endothelial barrier, resulting in capillary leakage and loss of protein, inflammatory cells and large volumes of fluid into the interstitial space. The precise mediators of this capillary leakage are still being discovered and currently include: endotoxin from Gram-negative bacteria; cytokines—TNF-α and IL-6; arachidonic acid metabolites—leukotrienes and prostaglandins; complement components C3a and C5a; other vasoactive peptides—bradykinin, histamine; chemokines—macrophage inflammatory protein 1α.[63,64]

The normal transcapillary escape rate for albumin increases by up to 300% in patients with septic shock, and by 100% after cardiac surgery. In septic patients, the transcapillary exchange rate may well improve with appropriate treatment. With increased flow of albumin across capillary membranes, there should be an increase in lymphatic return to the intravascular compartment. Studies of albumin kinetics during major surgery have shown a reduction in the flow rate of lymph and the albumin concentration in lymph. It is not known if this extends into the postoperative period. Measurement of total circulating and total exchangeable albumin pools shows a 30% reduction with major surgery, consistent with sequestration of albumin into non-exchangeable sites, such as wounds, the intestine and extra-abdominal sites.[65,66]

The rate of albumin synthesis may be significantly altered in the critically ill. In the acute-phase response to trauma, inflammation or sepsis, there is an increase in the gene transcription rate for the positive acute-phase proteins such as C-reactive protein, and decreases in the rate of

transcription of albumin mRNA and the synthesis of albumin. IL-6 and TNF-α both act to reduce gene transcription. Induced inflammation in rats decreased the concentration of albumin mRNA and the rate of albumin synthesis, which reached a minimum by about 36 h and then began to rise again. A sustained inflammatory response in critical illness may lead to prolonged inhibition of albumin synthesis.[67,68,69]

Serum albumin appears to be a reliable prognostic indicator in various contexts. A recent review suggests that serum albumin could be an independent predictor of mortality in a wide range of clinical and research settings. It reports an estimated increase in the odds of death from 24 to 56% for each 2.5 g/l decrease in serum albumin concentration over the range of studies reviewed. Large community-based studies have shown a link between low serum albumin and an increase in morbidity and mortality. Albumin concentrations may be a marker for subclinical disease in elderly patients. In studies of hospitalized patients, hypoalbuminaemia is associated with increased length of stay, higher complication rates and higher mortality. In one study, a serum albumin concentration of less than 34 g/l was associated with a 30-day mortality rate of 24.6%. This increased to 62% if the serum albumin concentration was 20 g/l or less.[70,71]

The prognostic value of serum albumin extends to critically ill patients. A low serum albumin concentration correlates with increased length of stay in the intensive care unit (ICU) and with complication rates, such as ventilator dependency and the development of new infection. The daily trend of serum albumin can be a useful tool in predicting the weaning capability of patients needing mechanical ventilation.[72,73]

Non-survivors of critical illness have lower serum albumin concentrations than survivors. In one study, non-survivors had lower serum albumin concentrations on admission to the ICU, and their albumin concentrations decreased more rapidly in the first 24–48 h. The albumin concentration on admission was not a sensitive indicator of outcome, but the value at 24–48

h was as accurate as the APACHE II score in predicting mortality. The APACHE II system does not include serum albumin concentration as an independent predictor, and it has been found to be poorly predictive in hypoalbuminaemia. The APACHE III system does include serum albumin concentration, and it is more predictive of mortality in critical illness.[74,75,76]

A significant difference has also been shown between serum albumin concentrations of non-survivors and survivors of prolonged critical illness. Patients who were in the ICU for 7 days or more and survived had higher mean serum albumin concentrations than non-survivors, and were able to recover to a higher mean serum albumin concentration than non-survivors. Significantly, there was no difference between the COPs of the two groups.[77]

It has been shown that severe injury leads to a decrease in serum albumin, increased energy consumption, and increased net catabolism of total body protein roughly in proportion to the magnitude of the injury. The rapidity of the decrease suggests that the prime cause is due to redistribution and this seems to be confirmed by studies showing a several fold increase in the transcapillary escape rate.[78,79]

Pre-operative hypoalbuminaemia is a marker of malnutrition and a predictor of poor outcome. The clinical relevance of postoperative hypoalbuminaemia is less clear. Analysis of factors affecting serum albumin in patients during the five days following uncomplicated major (aortic) surgery indicated that some 18% of the decrease was due to hemorrhage, 6% due to increased catabolism and 77% due to re-distribution. The mean reduction in albumin in this group was maximal at 24 hours, when concentrations had decreased by 12 g/l. By day five the concentrations had returned to within 7 g/l of the pre-operative value.[80]

This study also demonstrated an increase in serum albumin postoperatively in the face of a negative nitrogen balance, which the authors concluded was in keeping with a minimal net catabolism of albumin at the expense of other proteins (especially muscle). A decrease

in serum albumin and an increased transcapillary escape rate were also demonstrated in a study where a disproportionate loss of plasma compared to blood was seen following abdominal surgery.[81]

In more recent studies, investigators have focused on the influence of albumin on duration of ICU stay and rate of recovery. A prospective randomized study of albumin versus gelatin solutions for routine fluid replacement in 475 ICU patients did not show any significant differences between duration of stay, complications or outcomes in the two groups. There are several other studies which failed to show a benefit in using albumin solutions although in all of these studies it was clear that the serum albumin values remained elevated.[82,83]

Considering that very few biomarkers of head injury are clinically available, it is imperative to study each in relation to neurological outcome.[84]

FiroozSalehpoor et al studied Prognostic Serum Factors in Traumatic Brain Injury in relevant publications from 2005 to 2014. Sixty-three studies were included. Most studies used Glasgow Outcome Score at 6 months post-injury as outcome measure, sometimes in combination with other outcome measures. Strong evidence for predicting outcome was found for serum concentration of S100 protein, NSE, MBP, NF-H, GFAP, UCH-L1, blood glucose levels, serum levels of LDH, sodium level, prothrombin time, partial thromboplastin time, platelet count, D.dimer, HSP 70, serum levels of IL-8, number of circulating EPCs, and DNA levels in serum. Moderate evidence for predicting outcome was found for high serum MMP9. Strong evidence of no association was found for WBC count and serum cortisol levels. Moderate evidence of no association was found for serum total cholesterol for other determinants, inconclusive or no evidence or limited evidence was found concluding S100 protein, NSE, MBP, NF-H, GFAP, UCH-L1, blood glucose levels, serum levels of LDH, sodium level, prothrombin time, Partial thromboplastin time, platelet count, D.dimer, HSP 70, serum levels of IL-8, number of circulating EPCs, and

DNA levels in serum predicted outcome after traumatic brain injury. WBC count, serum cortisol levels, total cholesterol and MMP9 did not have predictive value.[1]

Choon Hong Kan et al studied Prognostic Factors of Severe traumatic Brain injury Outcome in children aged 2-16 Years. 146 children with severe TBI (coma score less than 8) were evaluated in an attempt to establish the prognostic factors of severe TBI in children. The severity of TBI was assessed via modified Glasgow Coma Score for those more than 3 years old and via Children Coma Score for those under 3 years old. Clinical presentations, laboratory parameters and features of Computerised Tomography brain scans were analyzed. Outcomes were assessed at 6 months with the Pediatric Cerebral Performance Categories Scale; the outcomes were categorised as good or poor outcomes. Correlations with outcome were evaluated using univariate and multivariate logistic models. A low coma score upon admission was independently associated with poor outcome. The presence of diabetes insipidus within 3 days post-TBI (OR: 1.9), hyperglycaemia (OR: 1.2), prolonged PT ratio (OR: 2.3) and leukocytosis (OR: 1.1) were associated with poorer outcome.[85]

Cellular injury mediators such as Interleukins and tumor Necrosis Factor and positive acute phase reactants such as C reactive protein, Alpha – 1 acid glycoprotein and Alpha – 1 antitrypsin are not tested routinely in developing countries. Serum Albumin, because of it's low cost and critical physiological role, is emerging as a valuable prognostic marker of head injury in the present era. Head injury initiates a complex metabolic sequelae, some of which are seen uniformly in all patients of trauma and burns. Fleck et al, found the main cause of hypoalbuminemia in systemic injury to be due to increased vascular permeability.[86,87]

McClain et al demonstrated that the cytokine interleukin-6 (IL-6) plays a major role in initiating the acute phase response, especially in the production of acute phase reactants such as C-reactive protein. The

objectives of their study were to determine whether plasma or ventricular fluid IL-6 levels were elevated at time of admission after head injury and whether plasma IL-6 levels related temporally to clinical improvement or levels of acute phase reactants. Thirty patients with Glasgow Coma Scale (GCS) scores of 3 through 10 were observed for 15 days after head injury. Peak elevation of plasma IL-6 occurred on admission (85 ± 12 U/ml; normal level is less than 2 U/ml) and then decreased during the hospital course to a level of 29 ± 4 U/ml on day 15. Plasma IL-6 levels decreased significantly faster in patients with admission peak 24-hour GCS scores of 8 through 10 compared with patients with GCS score <8 ($p < 0.01$). Patients had markedly elevated and variable ventricular fluid IL-6 levels on admission (mean 3880 ± 2022 U/ml; normal, <2 U/ml). A temporal relationship was found between plasma IL-6 levels and multiple acute phase reactants thought to be mediated by IL-6. McClain et al concluded that plasma and ventricular fluid levels of IL-6 are elevated after head injury and that plasma IL-6 level is temporally related to acute phase reactants and clinical improvement. They suggested that IL-6 may play an etiologic role in many of the metabolic or nutritional sequel of head injury.[88]

Dhandapani et al assessed the prognostic significance of admission serum albumin levels in patients of head injury by conducting a prospective cohort study with control group. Within 24 hours of head injury, 154 patients underwent serum analysis for albumin along with 38 normal volunteers, studied in relation to various factors and subsequently followed-up. Mean serum albumin in head injury and control were 3.24 and 4.15 g/dL respectively ($p < 0.001$). Admission albumin had significant positive correlation with Glasgow coma score (GCS) ($p < 0.001$). Hypoalbuminemia (≤ 3.5 g/dL) at admission was noted in 88%, 52% and 33% of patients with severe, moderate and mild head injury respectively ($p < 0.001$). Significantly lower albumin levels were observed in patients with associated systemic injury; those requiring surgical decompression and in

the elderly. Mortality at 1 month was 43% in patients with admission hypoalbuminemia as compared to 17% in those with normal albumin levels (odds ratio [OR] 3.7, p = 0003) Unfavorable outcome at 3 months was noted in 62% of patients with admission hypoalbuminemia as compared to 18% of those having normal albumin levels (OR 7.3, p < 0.001). In multiple logistic regression analysis, admission hypoalbuminemia emerged as an independent predictor for unfavorable outcome, in addition to age and GCS. They hence concluded that admission hypoalbuminemia is an effective indicator of the severity of head injury, and an independent predictor for unfavorable outcome at 3 months.[89]

SS Dhandapani et al 2010 studied biochemical changes in patients with severe traumatic brain injury, with respect to neurological outcome. Adult patients admitted within 24 hours of traumatic brain injury with Glasgow Coma Score 4-8, were prospectively studied for changes in various biochemical parameters. Outcome was assessed at 6 months. The mean serum albumin levels showed progressive fall till 2 weeks from 3.23 g/dL to nadir value of 2.86 g/dL, followed by mild increase to 2.99 g/dL at 3 weeks (p<0.001). The mean daily urine creatinine values demonstrated significant fall from 1255.4 mg/d to 1010.2 mg/d at 3 weeks (p<0.001). There was significant increase in mortality at 2 months among patients with atleast 15% fall in serum albumin and urine creatinine less than 1000 mg/d at 3 weeks (p < 0.005). Unfavorable outcome was noted in 12 out of 15, with at least 15% fall in serum albumin at 3 weeks, compared to 11 out of 25, with less than 15% fall in serum albumin (p=0.03). Unfavorable outcome was also noted in 16 out of 22, with low urine creatinine (<1000 mg/d) at 3 weeks, compared to 6 out of 17, with normal urine creatinine (p=0.02). In patients with severe TBI, unfavorable neurological outcome at 6 months was associated with 15% fall of serum albumin or low urinary creatinine at 3 weeks, more so with the former.[34]

Du Chen et al. studied 326 patients of TBI. They were divided into a favorable group (GOS: 3 to 5) and an unfavorable group (GOS: 1 to 2). Serum albumin and prealbumin were measured from vein blood within 24 h after admission. Ninety one (27.9%) patients were with poor outcome (GOS: 1 to 2). The unfavorable group had lower albumin and prealbumin (P,0.001). Albumin and prealbumin were both positively correlated with GCS (r = 0.489, P,0.001; r = 0.222, P, 0.001, respectively) and GOS (r = 0.518, P,0.001; r = 0.314, P,0.001, respectively). After adjustment for confounding factors, the odds ratios of albumin and prealbumin were 0.866, 95% CI: 0.829 to 0.904 and 0.990, 95% CI: 0.985 to 0.995, respectively. In subgroup of GCS#8 (n = 101), the crude and adjusted odds ratios of serum albumin were both statistically significant (P = 0.027, P = 0.033, respectively), while prealbumin were not (P = 0.553, P = 0.576, respectively). The study concluded that both serum albumin and prealbumin may be used as predictors for unfavorable outcome of TBI, but the performances are significantly different, and former is much better. Especially, in patients of severe TBI (GCS#8), serum albumin is determined as an independent predictor, while prealbumin seems to be with no predictive value.[26]

Serum albumin level has been correlated with outcome in various clinical situations. Albumin has multiple physiologic properties that could be beneficial in brain injury. The Lund therapy for elevated intracranial pressure uses albumin as part of its protocol and demonstrates favorable outcome. Bernard et al sought to find out if albumin is associated with outcome after traumatic brain injury to justify conducting a randomized trial. A retrospective study of traumatic brain injury patients was conducted. Characteristics known to influence outcome were included in a multiple logistic regression model to analyze predictors of poor outcome at 6 months.[90]

Data were available for 138 patients. The majority of patients (65%) had a severe injury (Glasgow Coma Scale score <9). Seventy percent of

patients had a favorable outcome. Albumin levels decrease considerably from normal values in the first few days after injury irrespective of outcome. Albumin remained <25 g/L for a longer period of time in patient with an unfavorable outcome (6 days vs. 3 days, p = 0.012). Multiple logistic regression analysis identified albumin levels, age, Glasgow Coma Scale score at admission, and Injury Severity Score as predictors of poor outcome.[90]

They concluded that serum albumin level seems to be an independent predictor of poor outcome. The model also identified classic predictors of poor outcome that tends to strengthen its adequacy. Because albumin level is the only modifiable factor influencing outcome, it seemed justified to carry out a randomized trial of the use of albumin in the treatment of brain injury.[90]

Dziedzic et al aim conducted a study to determine if relatively high serum albumin level was associated with decreased risk of poor outcome in ischemic stroke patients. Seven hundred fifty-nine consecutive patients with acute ischemic stroke were included. Functional outcome was measured 3 months after stroke using modified Rankin Scale (mRS). Poor outcome was defined as mRS>3 or death. Serum albumin level was measured within 36 hours after stroke onset. Patients with poor outcome had significantly lower serum albumin level than patients with favorableoutcome . They concluded that relatively high serum albumin level in acute stroke patients decreases the risk of poor outcome. The neuro-protective effects of endogenous albumin on the capillary microcirculation in the early reperfusion phase were proposed to explain the cellular mechanism of this association.[91]

Zhi-Yong Zhao et al 2016 studied Serum albumin as a predictor for duration of weaning in patients with traumatic brain injury. A retrospective study was conducted in the ICU of Huashan Hospital affiliated to Fudan University between January 2009 and June 2014. 104 patients suffering from traumatic brain injury were included. Serum albumin concentration,

Motor GCS score and other clinical and laboratory data were collected and analyzed. Serum albumin concentration was associated with duration of weaning, patients with higher albumin levels had shorter duration of weaning, either at admission (P = 0.002) or at weaning (P < 0.001). Lower albumin levels appeared to be more frequent in patients with epidural hematoma (P = 0.004). Serum albumin level seems to be an independent predictor for duration of weaning in patients with isolated traumatic brain injury. Therefore it is advisable that albumin can be used for clinical instruction for weaning in patients with isolated brain injury.[27]

Mithilesh Kumar Pandey et al 2016 studied serial estimation of serum albumin and its role in traumatic brain injury patients In the study 86 (43%) patients having hypoalbuminemia (< 3.5 gm/dl) and falling trend in admission serum albumin levels from day 1 to 10th day with decrement in GCS was statistically highly significant (p < 0.001) as hypoalbuminemia was noted in 68%, 39.65 and 33.43% patients with severe, moderate and mild head injury respectively. The present study was showed that female TBI patients having less no. of hypoalbuminemia compare to male as 77.7%, 45.4%, 31.4% male and 42.8%, 28.5%, 27.2% female having hypoalbuminemia (< 3.5 gm/dl) in severe, moderate and mild head injury respectively and statistically significant difference in severe and moderate group.[92]

SivaaRajendran et al 2017 Evaluated role of serum albumin as a prognostic marker in traumatic brain injury. Fifty four consecutive patients admitted to emergency intensive care with varying degrees of head injuries, were grouped into 3 categories based on the admission time Glasgow Coma Scale (GCS) as mild (13 to 15), moderate (9-12), and severe brain injury(8 or less) and their serum albumin were estimated. Out of 54 patients, 15 had hypoalbuminemia (albumin <3.5g/dL), while for the rest the levels were normal. In the normal albumin group 87% patients showed good outcome and only 13% showed poor outcome. With Kaplan-Meier survival curves, patients with normal albumin levels showed a

significantly higher chance to survive than patients with hypoalbuminemia. Further stratification of our cohort into groups according to the interquartile range of serum albumin and comparing it with their clinical outcome by Cox regression indicated that the probability of mortality increased with the decrease in serum albumin (hazard ratio[HR] = 0.15; 95% CI = 0.03- 0.6) with a significant p value of <0.05.[23]

MATERIALS AND METHODS

SOURCE OF DATA

Patients admitted to emergency and trauma center of Dayanand Medical College and Hospital Ludhiana during the period of February 2018 to July 2019 with severe traumatic brain injury having Glasgow coma score of less than equal to 8 were included in the study.

METHODS OF COLLECTION OF DATA

All the patients were evaluated neurologically and radiologically with non contrast CT of head. On admission the serum albumin of the patient was noted, appropriate management plan was decided based on examination and CT findings. Patients were managed in neurointensive care unit and neurosurgery ward with appropriate ventilator and ionotropic support as required.

Patient underwent serial assessment of their serum albumin at the day 1 (on admission), day 3, day 7 and day 10 of the stay irrespective of patient undergoing surgical or non surgical management.

The outcome of the patient was assessed according to Glasgow outcome score at the time of discharge. Patients weredivided into two groups, unfavourable (GOS grades-1,2,3) and favourable (GOS grades 4,5), the mean value of serum albumin was correlated to the outcome of the patients at discharge. The value of serum on admission was correlated with duration of stay in hospital, duration of ventilator support required, complications.

Inclusion criterion

1. Patients admitted with severe head injury GCS 8 or less
2. Head injury verified on CT or MRI

Exclusion criterion

1. Patients less than 18 years and more than 65 years
2. Polytrauma patients
3. Patients with hepatic disease, chronic renal failure and cardio-respiratory disease

Duration of study

Study was conducted from February 2018 to July 2019 on the patients admitted with severe traumatic brain injury

Management plan

Patients were managed according to the examination and radiological findings and appropriate management plan was decided whether surgical or non surgical. ICU care and ventilator and ionotropic support was given as required

Outcome

Outcome was assessed at the end of hospital stay by Glasgow outcome score, duration of stay, need for ventilator support, ionotropic support and complications will be analysed

Glasgow Outcome Scale (GOS)

Score	Term	Definition
1	Dead	No life
2	Vegetative state	Unaware of self and environment
3	Severe disability	Unable to live independently
4	Moderate disability	Able to live independently
5	Mild disability	Able to return to work/school

Statistical Analysis

Frequency distribution reported. Descriptive analysis done. Statistics reported as Mean ± SD and count as n (%). Student ‘t’ test and chi square test used. p value ≤0.05 consider as significant. Data analysed using intercooled stat 9.2 statistical software.

OBSERVATIONS & RESULTS

TABLE 1: AGE DISTRIBUTION OF PATIENTS

Age group	No. of cases	Percentage
<20	10	9.1%
21-30	25	22.7%
31-40	30	27.3%
41-50	26	23.6%
> 50	19	17.3%
Total	110	100.0%

Table showing percentage distribution of patients under various age groups. The majority of patients in our study belonged predominantly to the 31-40 years age bracket. The minimum number of patients were the ones below 20 years of age.

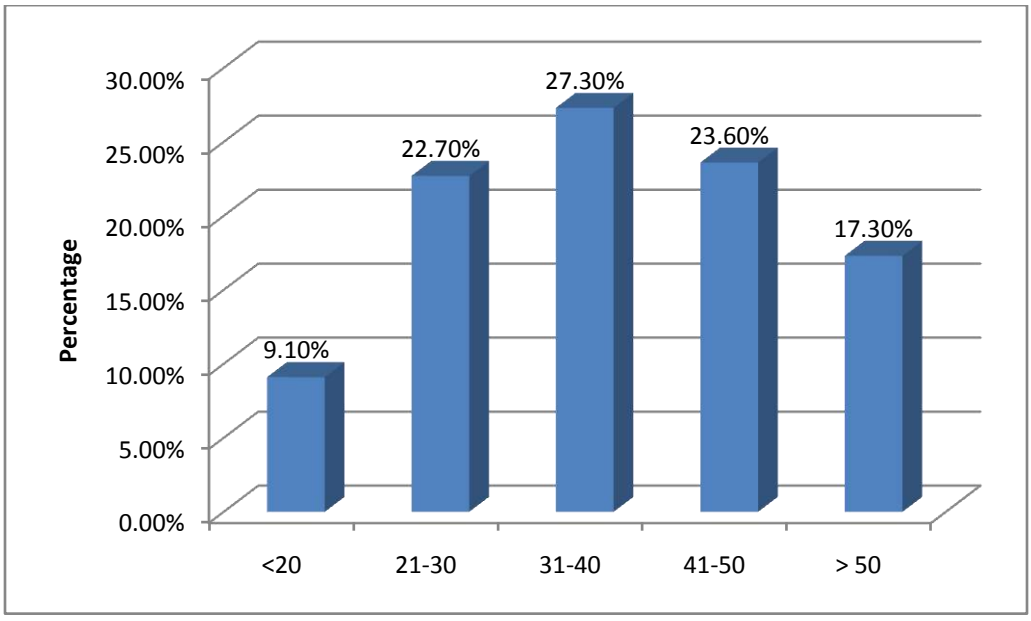

FIGURE 1: AGE DISTRIBUTION OF PATIENTS

TABEL 2: GENDER DISTRIBUTION OF PATIENTS

Sex	No. of cases	Percentage
Female (Fe)	25	22.7%
Male (M)	85	77.3%
Total	110	100.0%

The patients under study were predominantly males (77.3%),with female patients constituting only 22.7%.

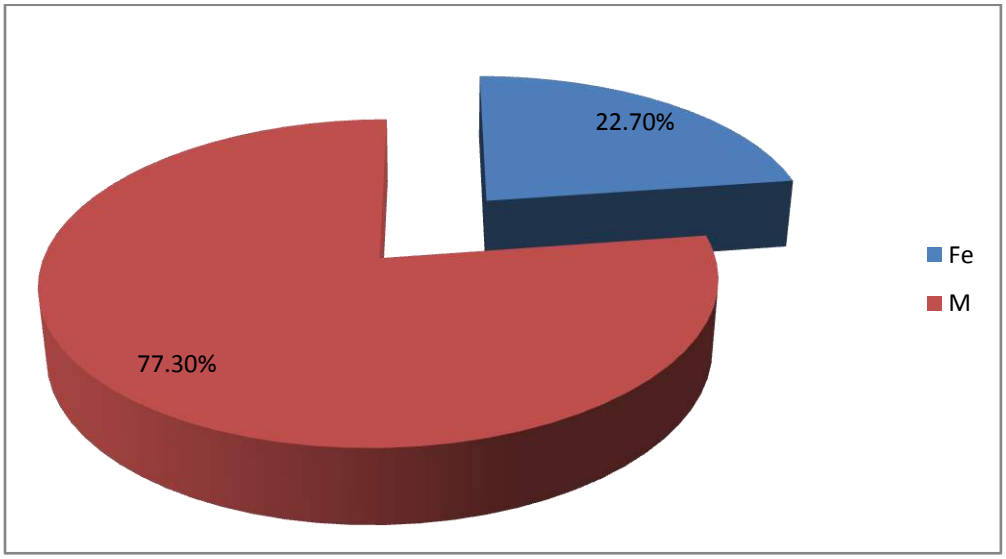

FIGURE 2: GENDER DISTRIBUTION OF PATIENTS

TABLE 3: MODE OF INJURY OF PATIENTS

MODE OF INJURY	No. of cases	Percentage
ASSAULT	11	10.0%
FALL	24	21.8%
RSA	75	68.2%
Total	110	100.0%

Majority of the patients admitted during the course of our study were injured in road traffic accidents (68.2%). Patients injured due to a fall from height constituted 21.0% patients. 10 % patients reported an alleged assault.

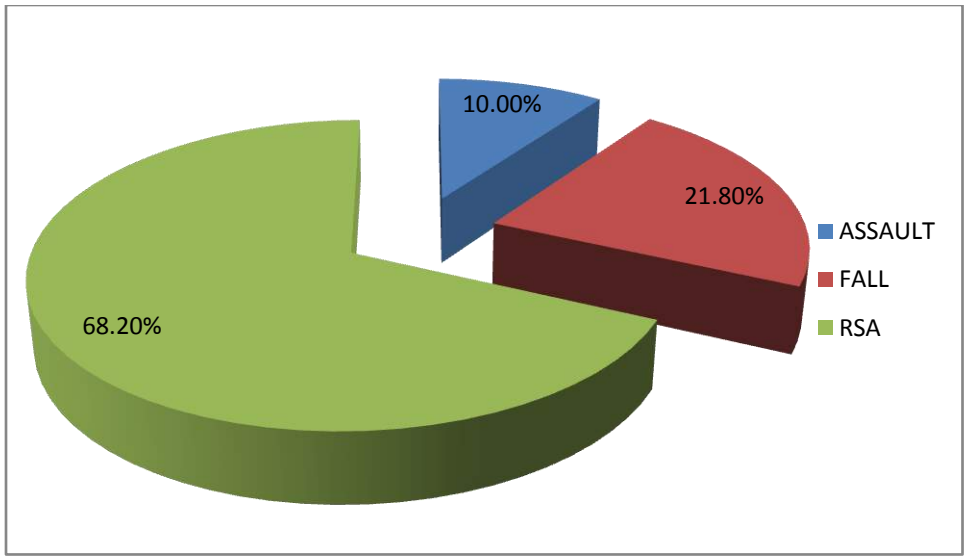

FIGURE 3: MODE OF INJURY OF PATIENTS

TABLE 4: AGE DISTRIBUTION VERSUS MODE OF INJURY

		MODE OF INJURY			Total	Chi-square value	p-value
		ASSAULT	FALL	RSA			
Age group	<20	1	3	6	10	2.667	0.953
	21-30	3	7	15	25		
	31-40	3	4	23	30		
	41-50	2	6	18	26		
	> 50	2	4	13	19		
Total		11	24	75	110		

Most of the patients in our study were injured due to road traffic accidents, with the majority road traffic accidents occurring in the fourth decade. Fall from height was most commonly seen in the fifth and sixth decade, owing to the higher incidence of falls among the aged. Alleged assault was observed in relatively few patients, with the majority being in the third and fourth decade. Mode of injury did not show any statistically significant correlation with age (p value = 0.953).

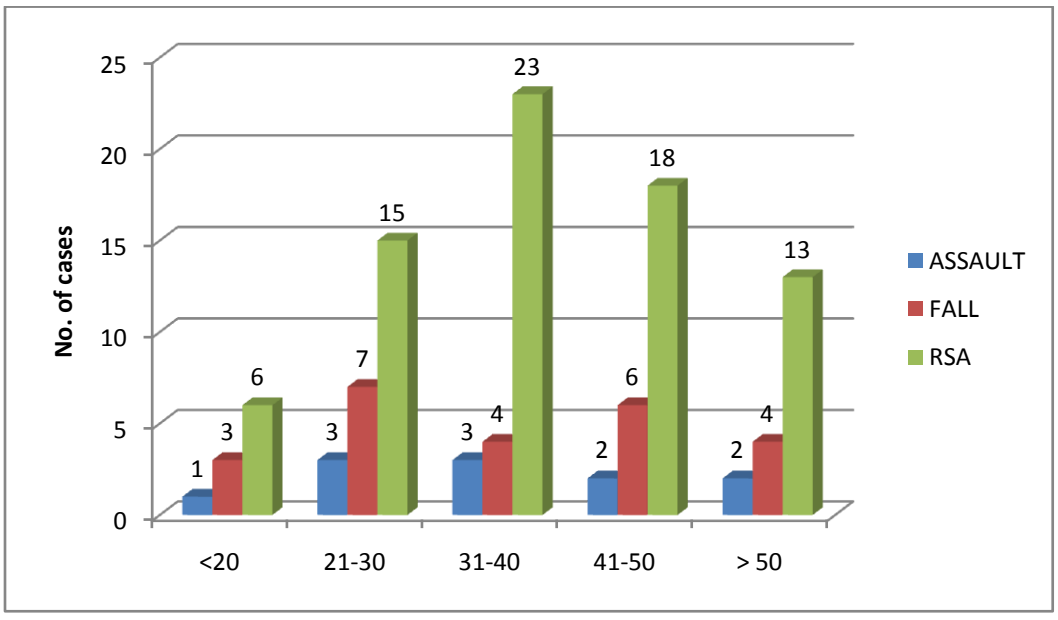

FIGURE 4: AGE DISTRIBUTION VERSUS MODE OF INJURY

TABLE 5: PATIENT DIAGNOSIS AND INJURY CODE

CT head findings code	No. of cases	Percentage
1	37	33.6%
2	29	26.4%
3	8	7.3%
4	6	5.5%
5	30	27.3%
Total	110	100.0%

Injury Code 1- Subdural Hemorrhage
Injury Code 2- Hemorrhagic Contusion
Injury Code 3- Intracerebral Hemorrhage
Injury Code 4- Extradural Hemorrhage
Injury Code 5- Miscellaneous Including DAI

Majority of patients in the study were diagnosed with subdural hemorrhage (33.6%). 26.4% patients had hemorrhagic contusions. Patients with intracerebral hemorrhage constituted 7.3%, 5.5% patients had extradural hemorrhage.

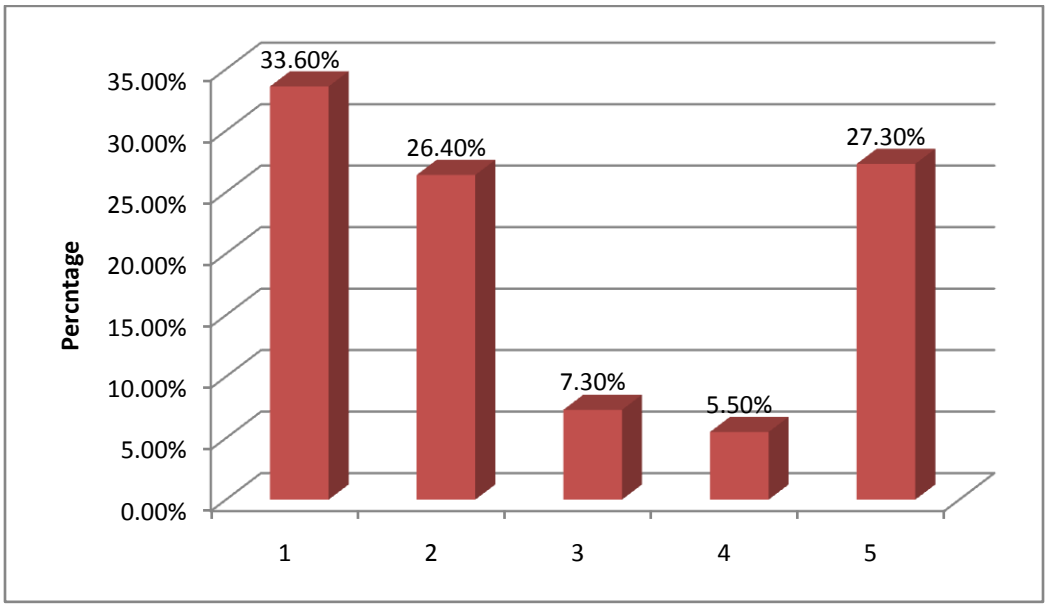

FIGURE 5: PATIENT DIAGNOSIS AND INJURY CODE

TABLE 6: PATIENT OUTCOME

OUTCOME GOS ON DISCHARGE(F/UF)	No. of cases	Percentage
F	32	29.1%
UF	78	70.9%
Total	110	100.0%

Out of 110 patients in our study 32(29.1%) patients had favorable outcome and 78 patients(70.9%) patients had unfavorable outcome

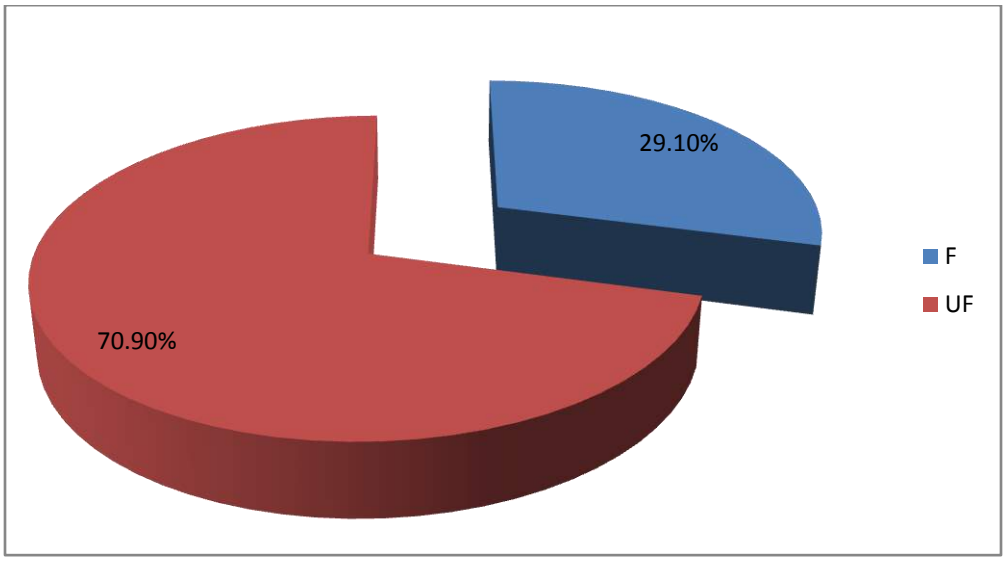

FIGURE 6: PATIENT OUTCOME

TABLE 7: COMPLICATION RATE

COMPLICATIONS	No. of cases	Percentage
No (N)	77	70.0%
Yes (Y)	33	30.0%
Total	110	100.0%

Out of total 110 patients, 33 (30%) patients had complication like respiratory tract infections urinary tract infection, wound related infections, cardiac complications like acute myocardial ischemia, renal complications like acute kidney injury etc. 77 patients(70%) Had no complication.

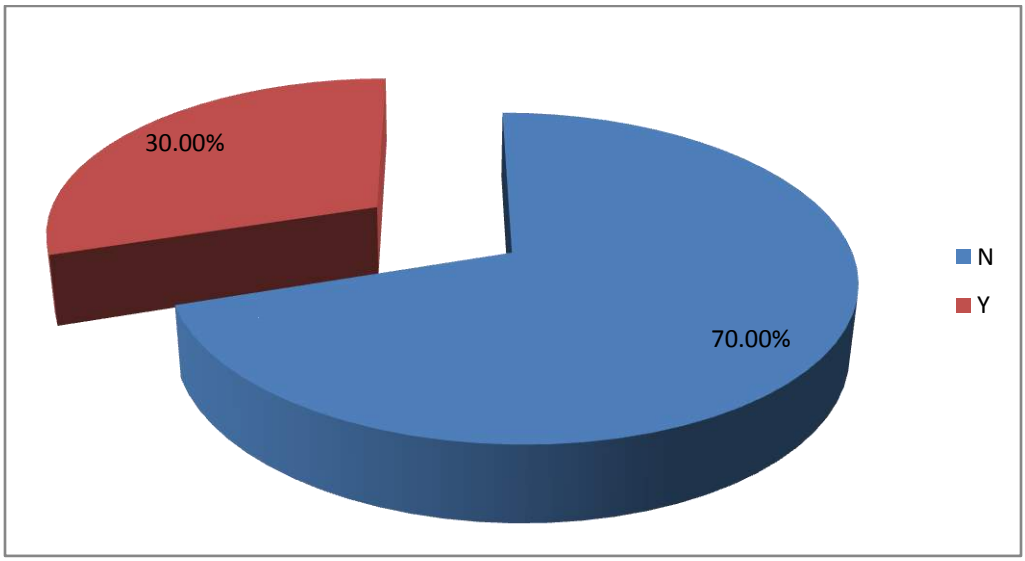

FIGURE 7: COMPLICATION RATE

TABLE 8: PATIENT MANAGEMENT

MANAGEMENT	No. of cases	Percentage
Conservative (C)	39	35.5%
Surgical (Su)	71	64.5%
Total	110	100.0%

Out of the total 110 patients 71 patients (64.5%) were managed with one or more surgical procedure, 39 patients (35.5%) patients were managed conservatively.

C= Conservative
Su= Surgical

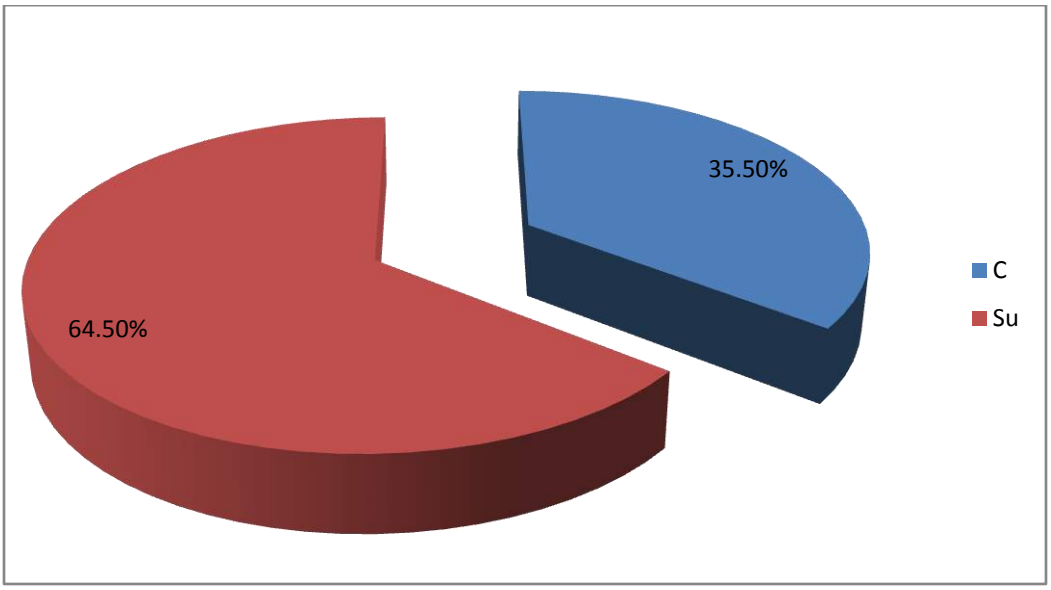

FIGURE 8: PATIENT MANAGEMENT

TABLE 9.1: AGE VS PATIENT OUTCOME

	F (n=32)		UF (n=78)		t	p-value
	Mean	SD	Mean	SD		
Age	37.59	14.13	38.58	12.20	-0.366	0.715

In our study patients with favorable outcome had mean age of 37.59 years with standard deviation of 14.3. In the unfavorable outcome group the mean age of patients was 38.58 years with standard deviation of 12.2.

On statistical analysis of different age groups no statistically significant correlation was present (table 9.2)

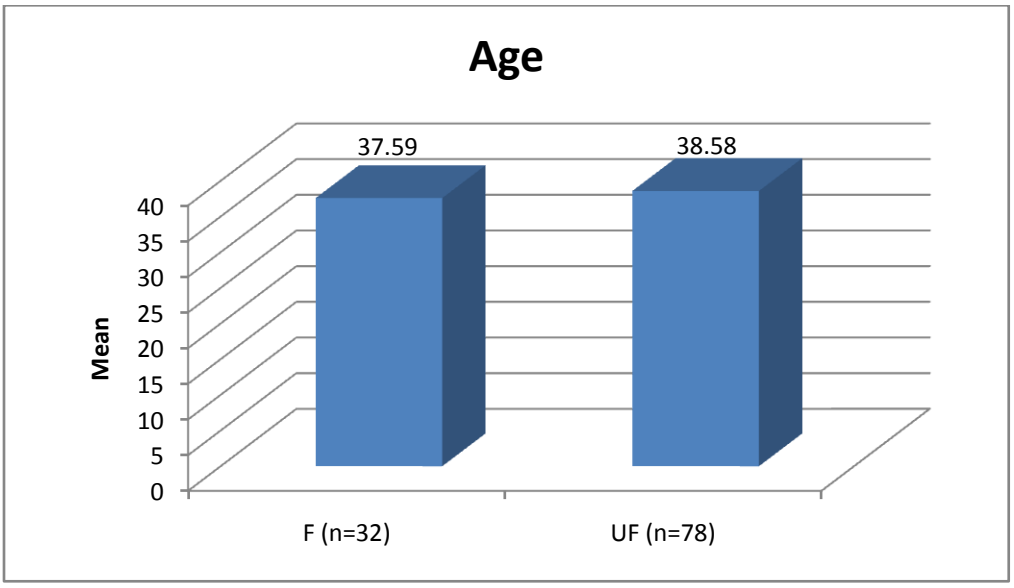

FIGURE 9.1: AGE VS PATIENT OUTCOME

TABLE 9.2: AGE DISTRIBUTION VS PATIENT OUTCOME

		OUTCOME GOS ON DISCHARGE(F/UF)				Total	Chi-square value	p-value
		F (n=32)		UF (n=78)				
Age group	<20	4	12.5%	6	7.7%	10	1.686	0.792
	21-30	7	21.9%	18	23.1 %	25		
	31-40	8	25.0%	22	28.2 %	30		
	41-50	6	18.8%	20	25.6 %	26		
	> 50	7	21.9%	12	15.4 %	19		

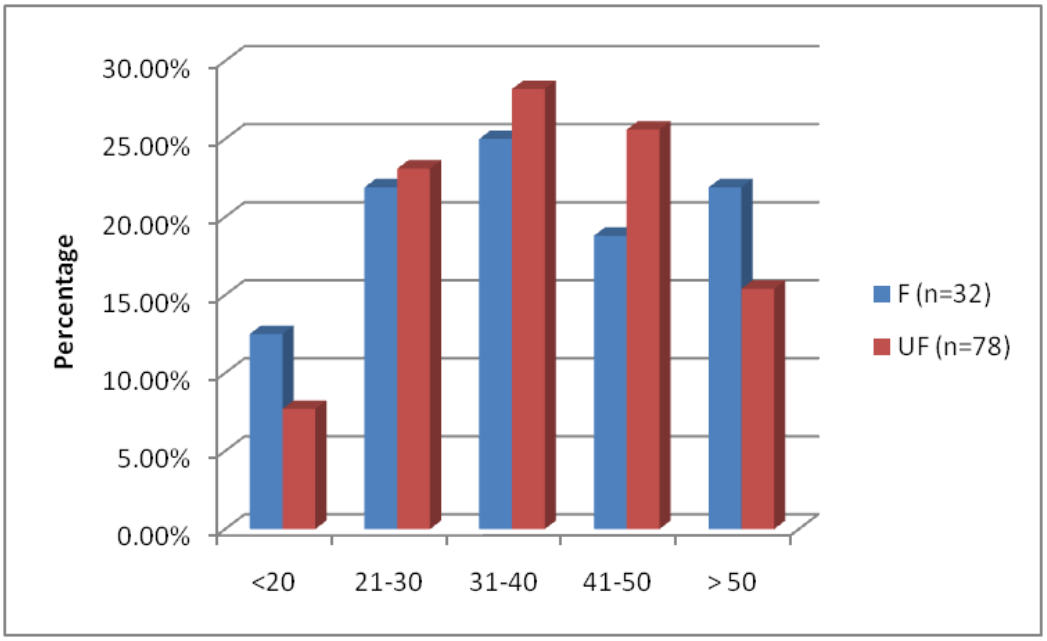

FIGURE 9.2: AGE DISTRIBUTION VS PATIENT OUTCOME

TABLE 10: GENDER VS PATIENT OUTCOME

		OUTCOME GOS ON DISCHARGE(F/UF)				Total	Chi-square value	p-value
		F (n=32)		UF (n=78)				
Sex	Female (Fe)	8	25.0%	17	21.8%	25	0.133	0.716
	Male (M)	24	75.0%	61	78.2%	85		

No statistically significant difference between gender and patient outcome

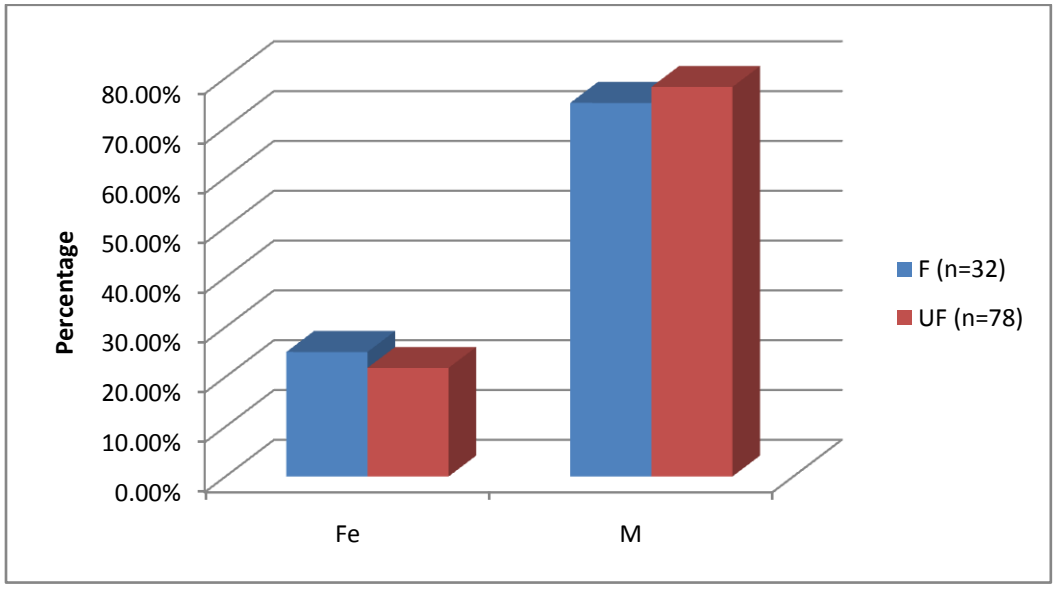

FIGURE 10: GENDER VS PATIENT OUTCOME

TABLE 11: DIAGNOSIS PATIENT INJURY CODE VS OUTCOME

		OUTCOME GOS ON DISCHARGE(F/UF)				Total	Chi-square value	p-value
		F (n=32)		UF (n=78)				
CT head findings code	1	9	28.1%	28	35.9%	37	1.228	0.873
	2	10	31.3%	19	24.4%	29		
	3	3	9.4%	5	6.4%	8		
	4	2	6.3%	4	5.1%	6		
	5	8	25.0%	22	28.2%	30		

INJURY CODE 1- SUBDURAL HAEMORRHAGE
INJURY CODE 2- HEMORRHAGIC CONTUSION
INJURY CODE 3- INTRACEREBRAL HEMORRHAGE
INJURY CODE 4- EXTRADURAL HEMORRHAGE
INJURYCODE 5- MISCELANEOUS INCLUDING DAI

No significant correlation between diagnosis and patient outcome

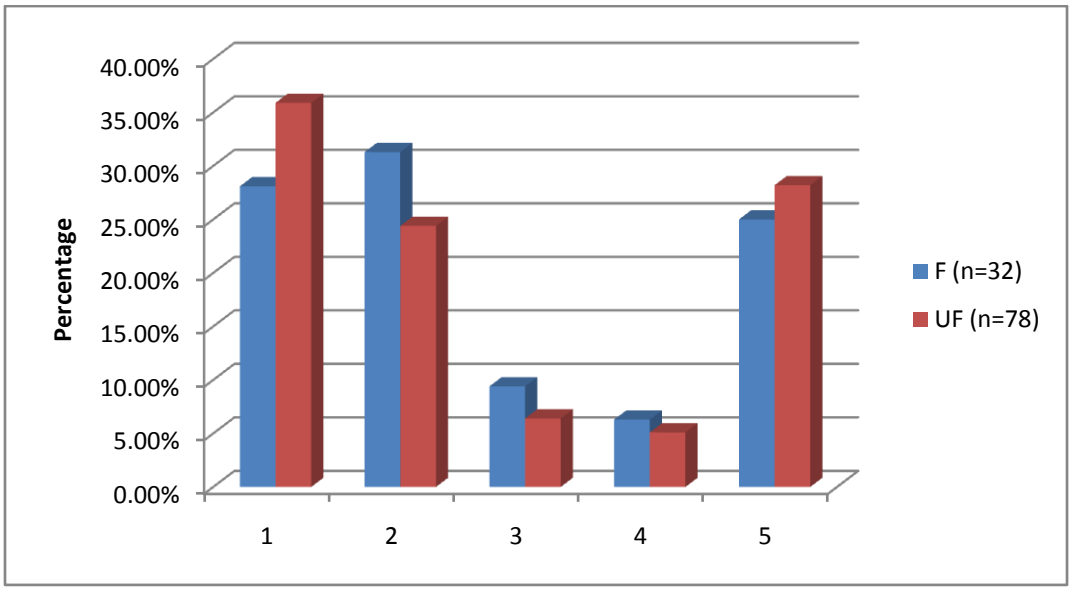

FIGURE 11: DIAGNOSIS PATIENT INJURY CODE VS OUTCOME

TABLE 12: MODE OF INJURY VS PATIENT OUTCOME

		OUTCOME GOS ON DISCHARGE(F/UF)				Total	Chi-square value	p-value
		F (n=32)		UF (n=78)				
MODE OF INJURY	ASSAULT	3	9.4%	8	10.3%	11	0.303	0.860
	FALL	6	18.8%	18	23.1%	24		
	RSA	23	71.9%	52	66.7%	75		

RSA- ROAD SIDE ACCIDENT

There was no statistically significant relation between mode of injury and patient outcome (p value = 0.860)

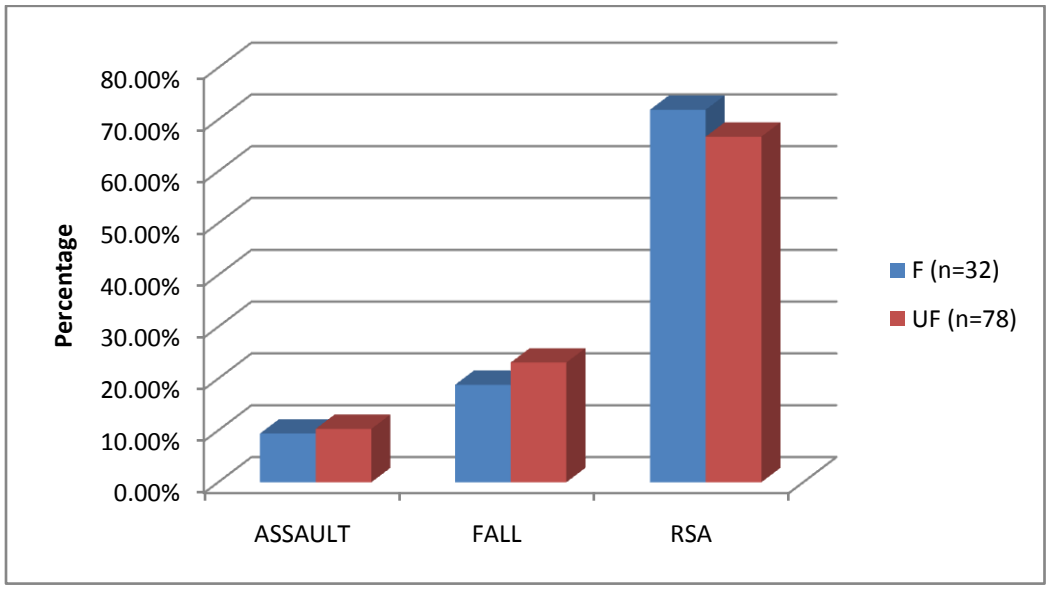

FIGURE 12: MODE OF INJURY VS PATIENT OUTCOME

TABLE 13: AGE DISTRIBUTION VS MODE OF INJURY

		MODE OF INJURY			Total	Chi-square value	p-value
		ASSAULT	FALL	RSA			
Age group	<20	1	3	6	10	2.667	0.953
	21-30	3	7	15	25		
	31-40	3	4	23	30		
	41-50	2	6	18	26		
	> 50	2	4	13	19		
Total		11	24	75	110		

No statistically significant difference between different age distribution and mode of injury was found in our study

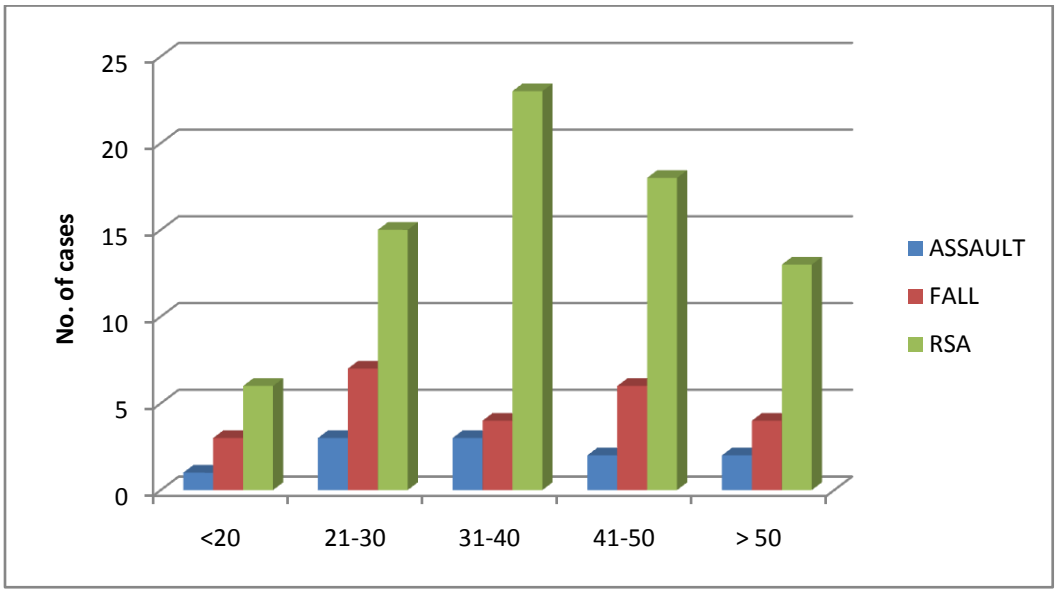

FIGURE 13: AGE DISTRIBUTION VS MODE OF INJURY

TABLE 14: TOTAL SERUM PROTEIN (TSP) ON ADMISSION VS OUTCOME

	F (n=32)		UF (n=78)		t	p-value
	Mean	SD	Mean	SD		
TSP ON ADMISSION	6.05	0.09	5.95	0.09	5.373	0.000

Mean serum total protein in favorable group was 6.0 with SD of 0.09, mean TSP on admission in unfavorable group was 5.95 with SD of 0.09.

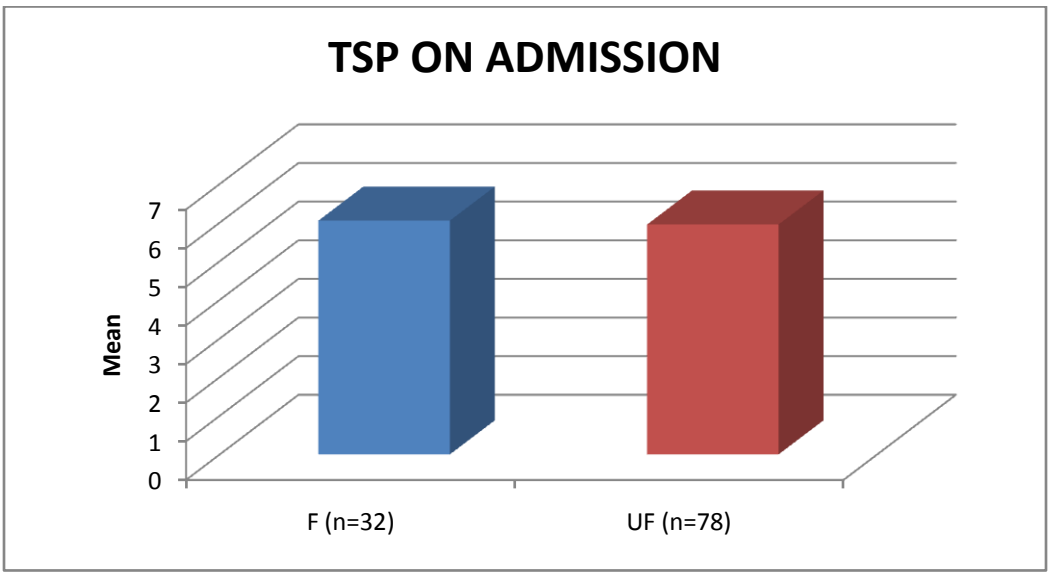

FIGURE 14: TSP ON ADMISSION VS OUTCOME

TABLE 15.1: POPULATION VS ADMISSION LEVELS OF SERUM ALBUMIN

S.ALB D1 GROUP	No. of cases	Percentage
Hypoalbumiminemia	69	62.7%
Normalalbuminemia	41	37.3%
Total	110	100.0%

In our study out of total 110 patients, 69 patients had admission serum albumin levels less than 3.5g/dl, 41 patients had serum albumin levels greater or equal to 3.4 g/dl

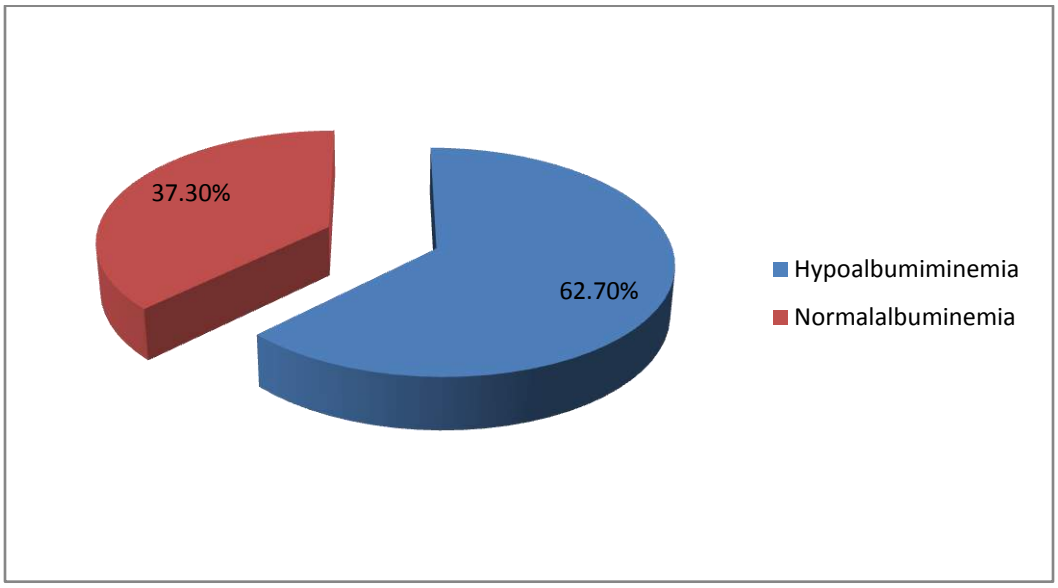

FIGURE 15.1: POPULATION VS ADMISSION LEVELS OF SERUM ALBUMIN

TABLE 15.2: POPULATION DISTRIBUTION VS ADMISSION LEVELS OF SERUM ALBUMIN

		S.ALB D1 GROUP		Total	Chi-square value	p-value
		Hypo	Normal			
Age group	<20	7	3	10	1.935	0.748
	21-30	17	8	25		
	31-40	16	14	30		
	41-50	16	10	26		
	> 50	13	6	19		
Total		69	41	110		

Table shows age distribution according to the levels of serum albumin, there is no statistically significant difference between different age groups

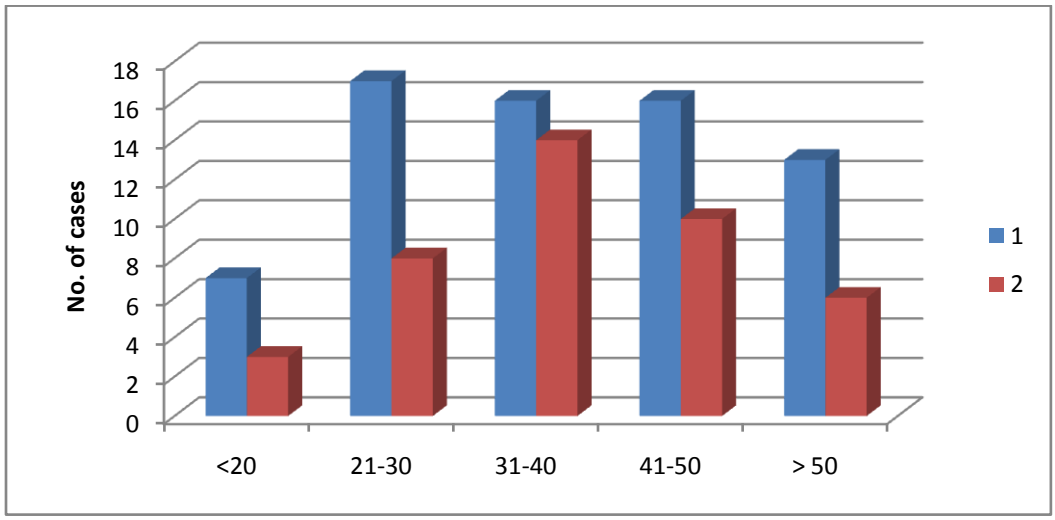

TABLE 15.2: POPULATION DISTRIBUTION VS ADMISSION LEVELS OF SERUM ALBUMIN

TABLE 16.1: SERUM ALBUMIN D1 VS OUTCOME

		OUTCOME GOS ON DISCHARGE(F/UF)				Total	Chi-square value	p-value
		F (n=32)		UF (n=78)				
S.ALB D1 GROUP	Hypo	8	25.0%	61	78.2%	69	27.473	0.000
	Normal	24	75.0%	17	21.8%	41		

In our study out of the total 110 patients 78 patients had unfavorable outcome, out of these 61 patients (78.2%) had hypo albuminemia and 17 patients (21.8%) had normal albumin levels at time of admission (D1). 32 patients had favorable outcome, out of these 24 patients (75%) had normal albumin levels and 8 patients (25%) had hypoalbuminemia.

On statistical analysis significant correlation was found between admission levels of serum albumin and outcome on discharge/ death

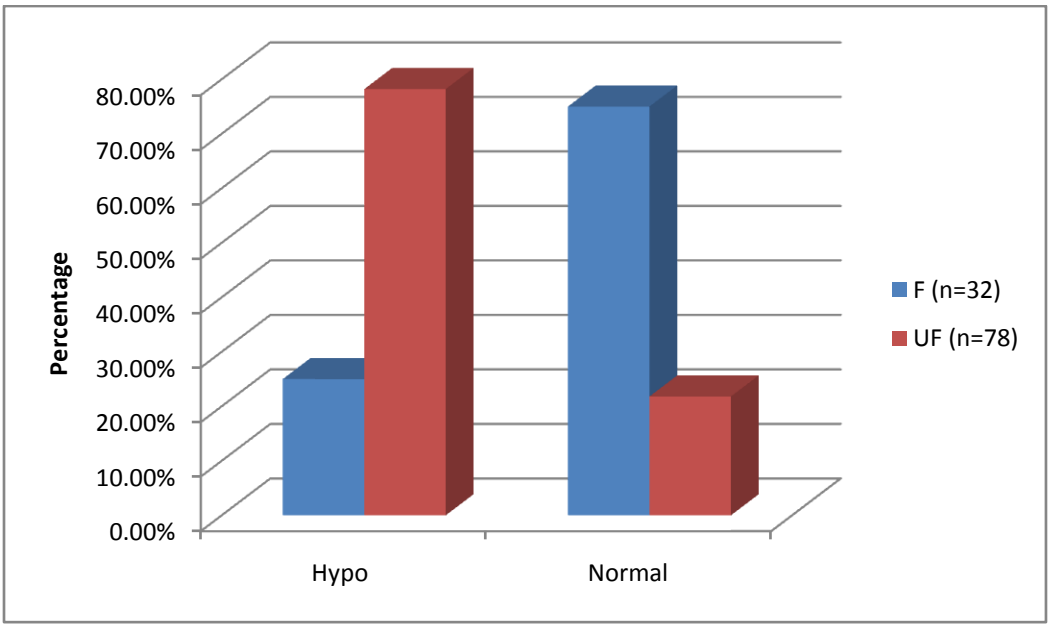

TABLE 16.1: SERUM ALBUMIN D1 VS OUTCOME

TABLE 16.2: MEAN SERUM ALBUMIN D1 VS OUTCOME

	F (n=32)		UF (n=78)		t	p-value
	Mean	SD	Mean	SD		
S.ALB D1	3.54	0.08	3.42	0.08	7.616	0.000

Mean serum albumin on admission was significantly higher in group with favorable outcome i.e 3.54 with SD of 0.08 as compared to group with unfavorableoutcome ie 3.42 with SD of 0.08.

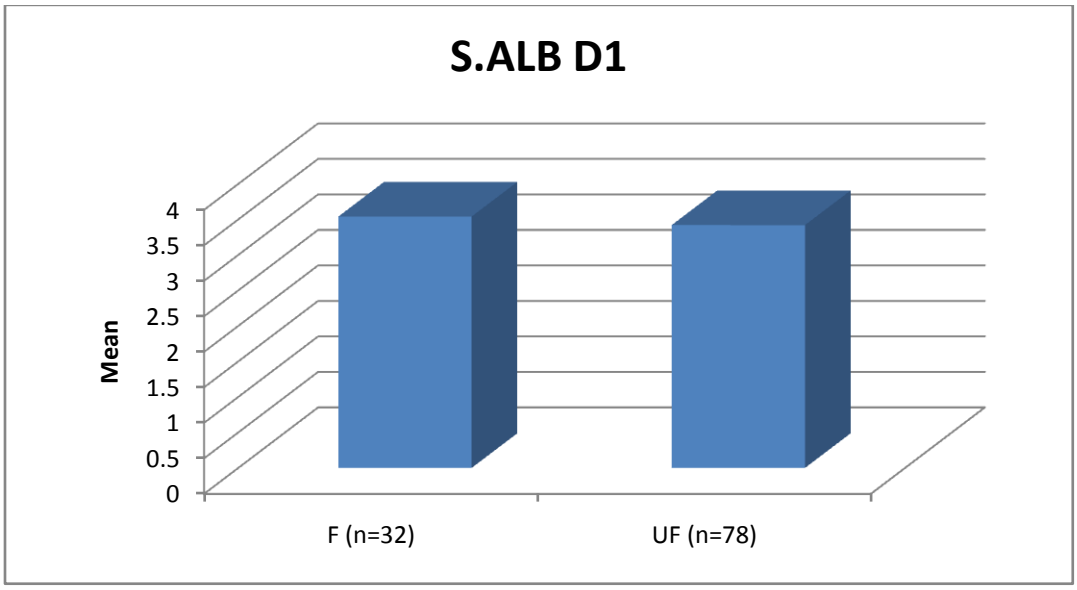

FIGURE 16.2: MEANSERUM ALBUMIN D1 VS OUTCOME

TABLE 17.1: MEAN SERUM ALBUMIN LEVELS OF STUDY POPULATION ON D1,D3,D7,D10

	N	Minimum	Maximum	Mean	Std. Deviation
S.ALB D1	110	3.2	3.7	3.5	0.1
S.ALB D3	110	3.1	3.5	3.3	0.1
S.ALB D7	110	3.0	3.5	3.2	0.1
S.ALB D10	110	2.8	3.5	3.1	0.2

Above table shows the mean levels of serum albumin of the study population at day 1,3,7,10. At day 1 mean serum albumin levels was 3.5 gm/dl with SD of 0.1, at day 3 mean serum albumin levels was 3.3gm/dl with SD of 0.1, on day 7 mean serum albumin levels was 3.2gm/dl with SD of 0.1, on day 10 mean serum albumin levels was 3.1gm/dl with SD of 0.2. Here we see that during the course of treatment there is decrease in the level of serum albumin in study population.

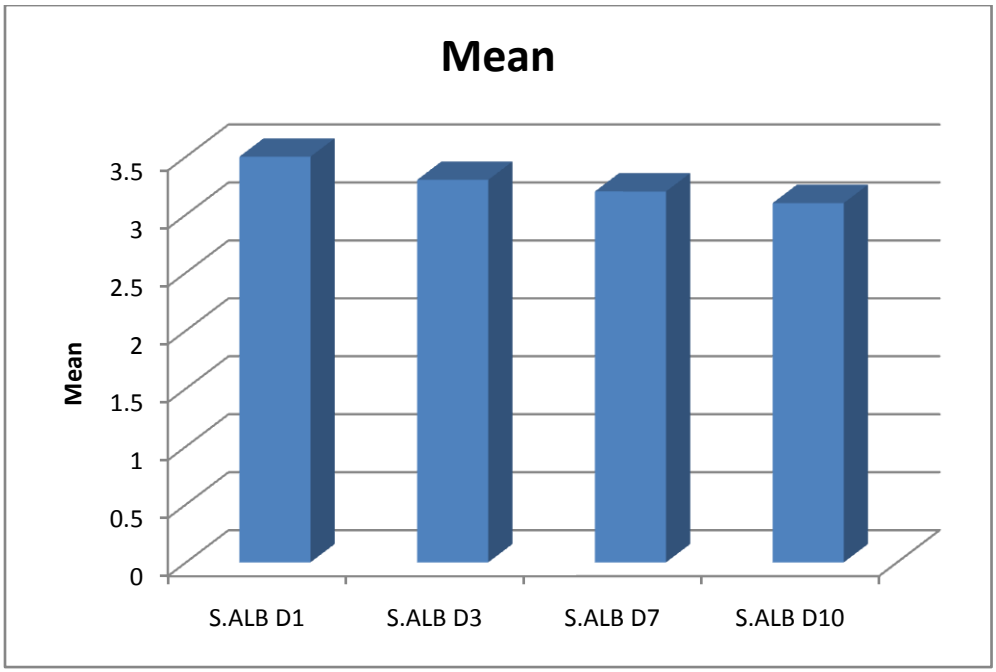

FIGURE 17.1: MEAN SERUM ALBUMIN LEVELS OF STUDY POPULATION ON D1, D3, D7, D10

FIGURE 17.2: PERCENTAGE FALL IN MEAN SERUM ALBUMIN LEVELS OF STUDY POPULATION ON D3 ,D7, D10

	N	Minimum	Maximum	Mean	Std. Deviation
Percentage fall D3	110	0.0	7.7	3.6	1.8
Percentage fall D7	110	1.4	15.4	6.6	2.9
Percentage fall D10	110	2.9	18.5	9.8	3.8

Table shows mean percentage fall in serum albumin at day 3, day 7, and day 10.

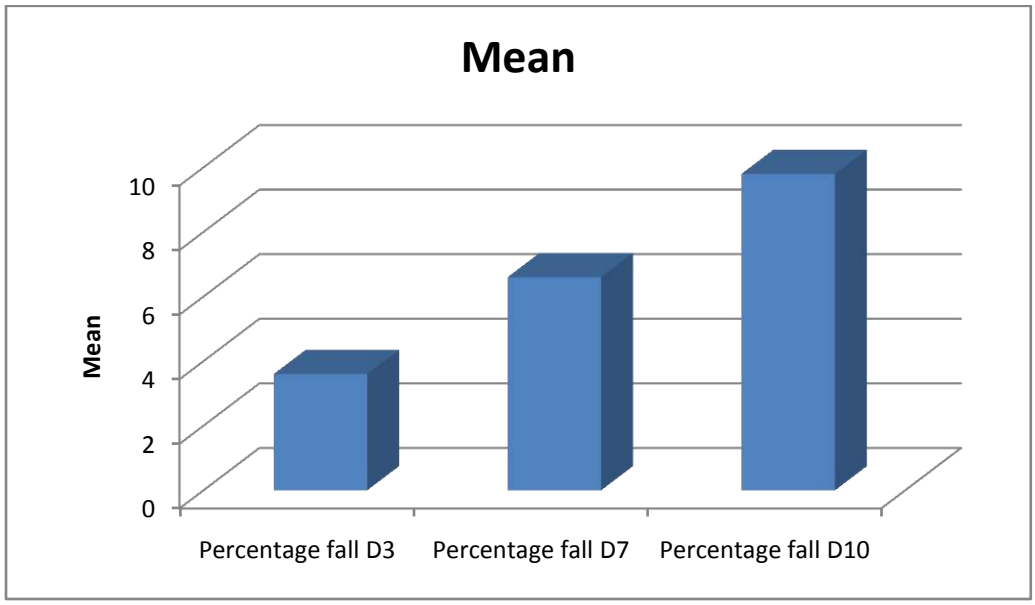

FIGURE 17.2: PERCENTAGE FALL IN MEAN SERUM ALBUMIN LEVELS OF STUDY POPULATION ON D3, D7, D10

TABLE 18:1POPULATION DISTTRIBUTION ACCORDING TO SURVIVAL/ NON SURVIVAL

SURVIVAL/NONSURVIVAL	No. of cases	Percentage
NS	13	11.8%
S	97	88.2%
Total	110	100.0%

S – Survival
NS – Non Survival

Out of total 110 patient in the study 97 patients (88.2%) survived, 13 Patients (11.8%) expired during course of treatment

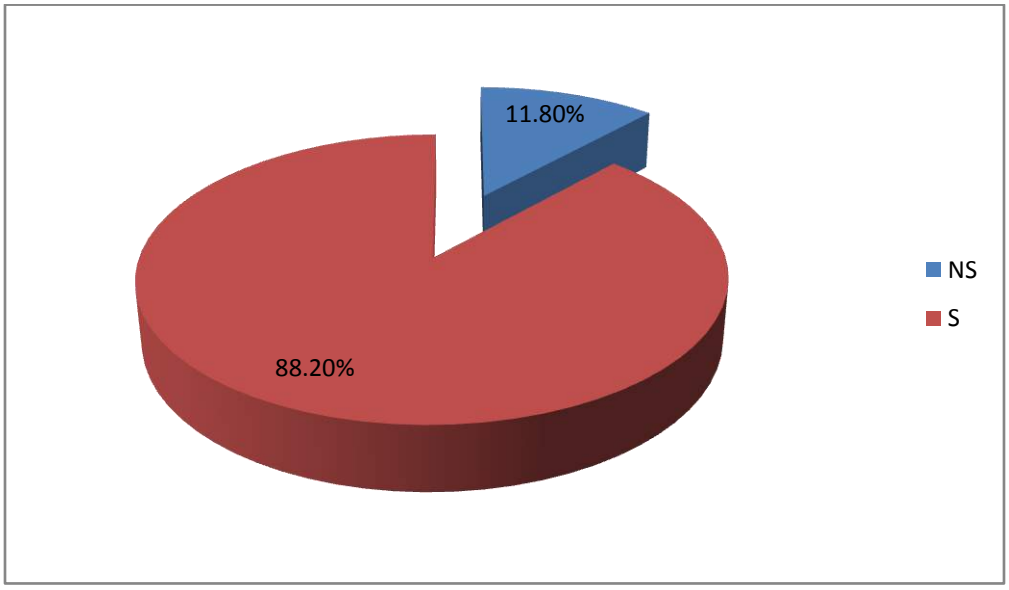

FIGURE 18.1: POPULATION DISTTRIBUTION ACCORDING TO SURVIVAL/ NON SURVIVAL

TABLE 18.2: MEAN SERUM ALBUMIN ON ADMISSION VS PATIENT SURVIAL

		SURVIVAL/NONSURVIVAL				Total	Chi-square value	p-value
		NS (n=13)		S(n=97)				
S.ALB D1 GROUP	Hypo	13	100.0%	56	57.7%	69	8.76	0.002
	Normal	0	0.0%	41	42.3%	41		

Table shows distribution of survival and non survival population according to the level of serum albumin into hypo and normal groups

Out of 97 patients who survived 56 (57.7%) had hypoalbuminemia and 41 (42.3%) patients had normal level of serum albumin at the time of admission. All the non survival group patients had hypoalbuminemia.

On statistical analysis significant correlation was found between survival and admission level of serum albumin with p value of 0.002.

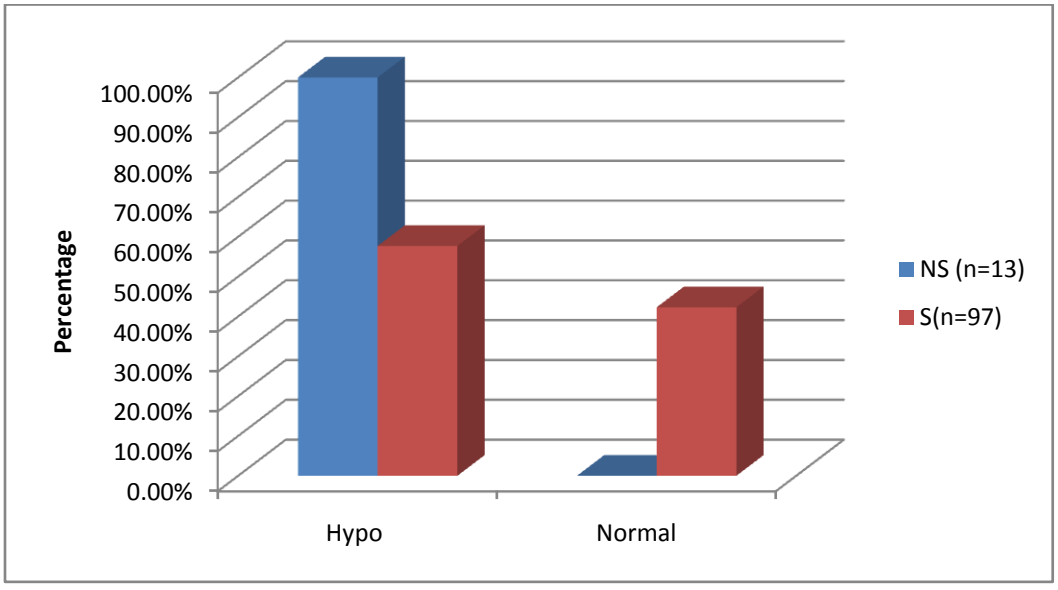

TABLE 18.2: MEAN SERUM ALBUMIN ON ADMISSION VS PATIENT SURVIAL

TABLE 18.3: MEAN SERUM ALBUMIN IN SURVIVAL AND NON SURVIVAL GROUPS

	NS (n=13)		S(n=97)		t	p-value
	Mean	SD	Mean	SD		
S.ALB D1	3.37	0.06	3.47	0.09	-3.364	0.001

Table shows mean serum albumin levels on admission (D1) between survival and non survival group

Mean serum albumin level on admission of survival group was 3.47mg/dl with SD of 0.09 and that of non survival group was 3.37mg/dl with SD of 0.06.

On statistical analysis significant correlation was found to be existing between patient survival and mean levels of serum albumin on admission with p value of 0.001.

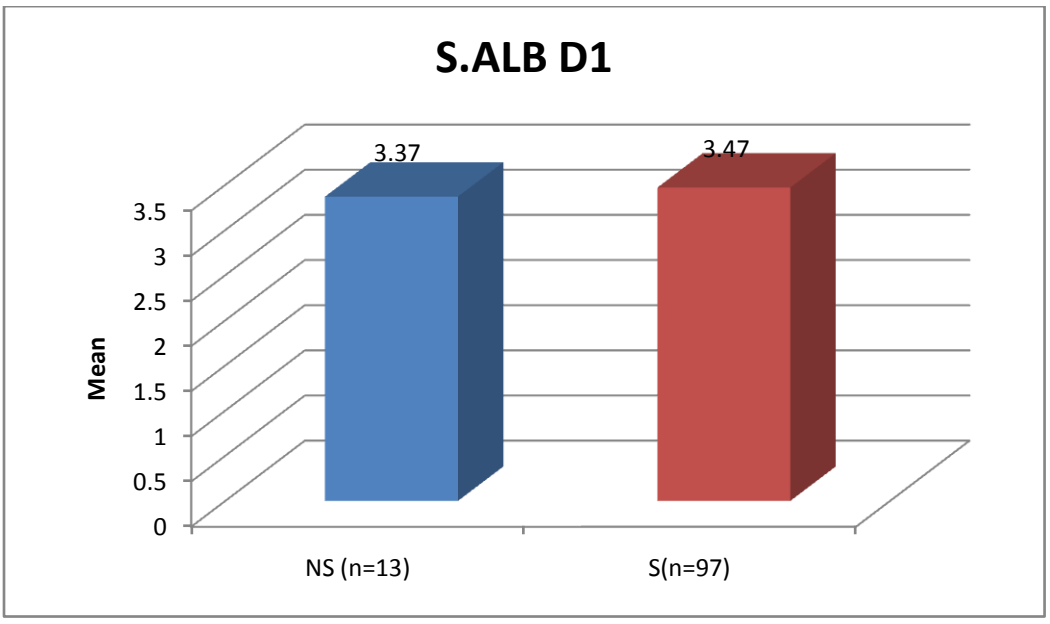

FIGURE 18.3: MEAN SERUM ALBUMIN IN SURVIVAL AND NON SURVIVAL GROUPS

TABLE 19: PERCENTAGE FALL IN SERUM ALBUMIN DAY 3 VS PATIENT OUTCOME

	F (n=32)		UF (n=78)		t	p-value
	Mean	SD	Mean	SD		
Per fall D3	2.44	1.12	4.02	1.78	-4.663	0.000

Table shows percentage fall in serum albumin at day 3 of the study with respect to patient outcome

Out of the total 110 study population 32 patients had favorable outcome and 78 had unfavorable outcome. Among the 32 patients with favorable outcome the percentage fall in serum albumin at day 3 was 2.44% with SD of 1.12%. In the unfavorable group the percentage fall in serum albumin was 4.02% with SD of 1.78.

On statistical analysis Percentage fall in serum albumin by day 3 was found to be significantly higher among unfavorable population as compared to favorable group (p<0.001)

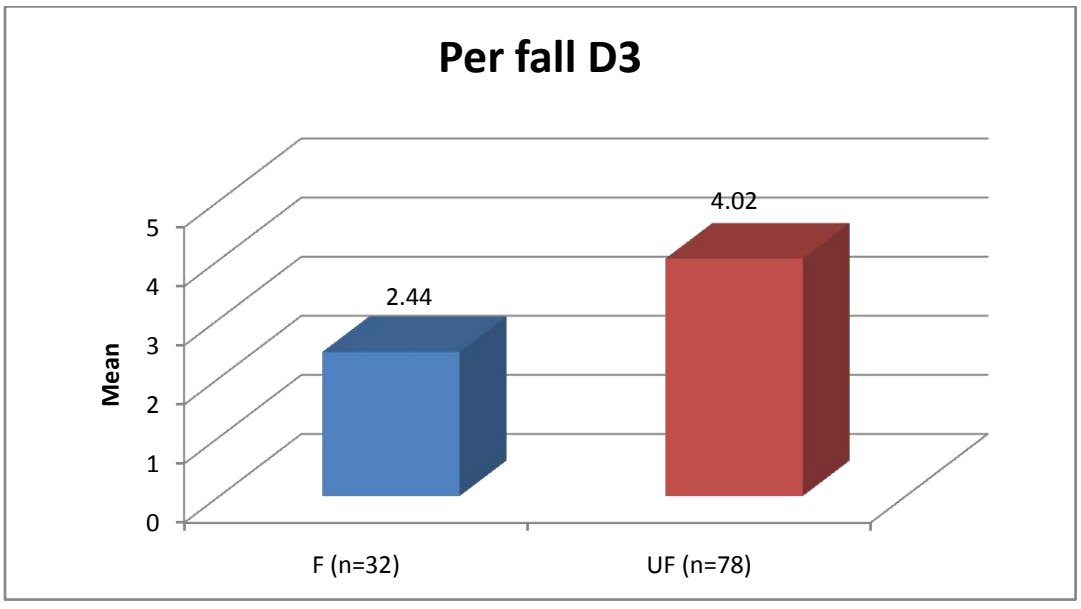

FIGURE 19: PERCENTAGE FALL IN SERUM ALBUMIN DAY 3 VS PATIENT OUTCOME

TABLE 20: PERCENTAGE FALL IN SERUM ALBUMIN DAY 7 VS PATIENT OUTCOME

	F (n=32)		UF (n=78)		t	p-value
	Mean	SD	Mean	SD		
Per fall D7	4.30	1.19	7.53	2.83	-6.217	0.000

Table shows percentage fall in serum albumin at day 7 of the study with respect to patient outcome

Out of the total 110 study population 32 patients had favorable outcome and 78 had unfavorable outcome. Among the 32 patients with favorable outcome the percentage fall in serum albumin at day 7 was 4.3% with SD of 1.19%. In the unfavorable group the percentage fall in serum albumin was 7.53% with SD of 2.83%.

On statistical analysis Percentage fall in serum albumin by day 7 was found to be significantly higher among unfavorable population as compared to favorable group ($p<0.001$)

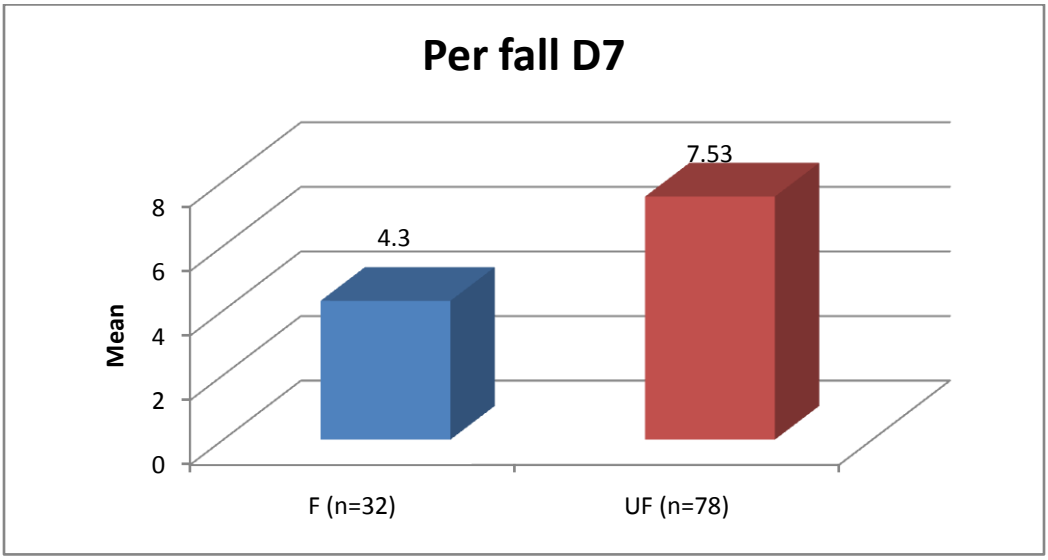

FIGURE 20: PERCENTAGE FALL IN SERUM ALBUMIN DAY 7 VS PATIENT OUTCOME

TABLE 21: PERCENTAGE FALL IN SERUM ALBUMIN DAY 10 VS PATIENT OUTCOME

	F (n=32)		UF (n=78)		t	p-value
	Mean	SD	Mean	SD		
Per fall D10	6.06	1.45	11.37	3.32	-8.704	0.000

Table shows percentage fall in serum albumin at day 10 of the study with respect to patient outcome

Out of the total 110 study population 32 patients had favorable outcome and 78 had unfavorable outcome. Among the 32 patients with favorable outcome the percentage fall in serum albumin at day 10 was 6.06 % with SD of 1.45 %. In the unfavorable group the percentage fall in serum albumin was 11.37% with SD of 3.32%.

On statistical analysis Percentage fall in serum albumin by day 10 was found to be significantly higher among unfavorable population as compared to favorable group (p<0.001).

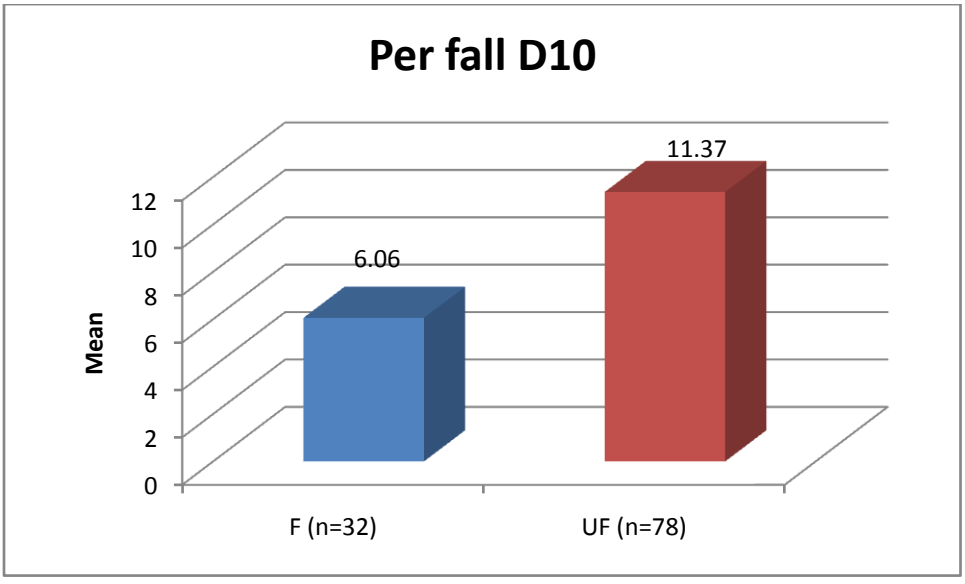

FIGURE 21: PERCENTAGE FALL IN SERUM ALBUMIN DAY 10 VS PATIENT OUTCOME

TABLE 22: PERCENTAGE FALL IN SERUM ALBUMIN DAY 3 VS PATIENT SURVIVAL

	NS (n=13)		S(n=97)		t	p-value
	Mean	SD	Mean	SD		
Per fall D3	4.49	1.36	3.44	1.78	2.042	0.044

Table shows percentage fall in serum albumin at day 3 of the study with respect to patient survival

Among the patients who did not survive (13 patients), the mean percentage fall in serum albumin by Day 3 was found to be 4.49% with SD of 1.36 %. The group with patients who survived showed a percentage fall in serum albumin of 3.34% with SD of 1.78%.

Percentage fall in serum albumin by day 3 was found to be significantly higher among non survivors. (p value<0.05) in comparison to survivors

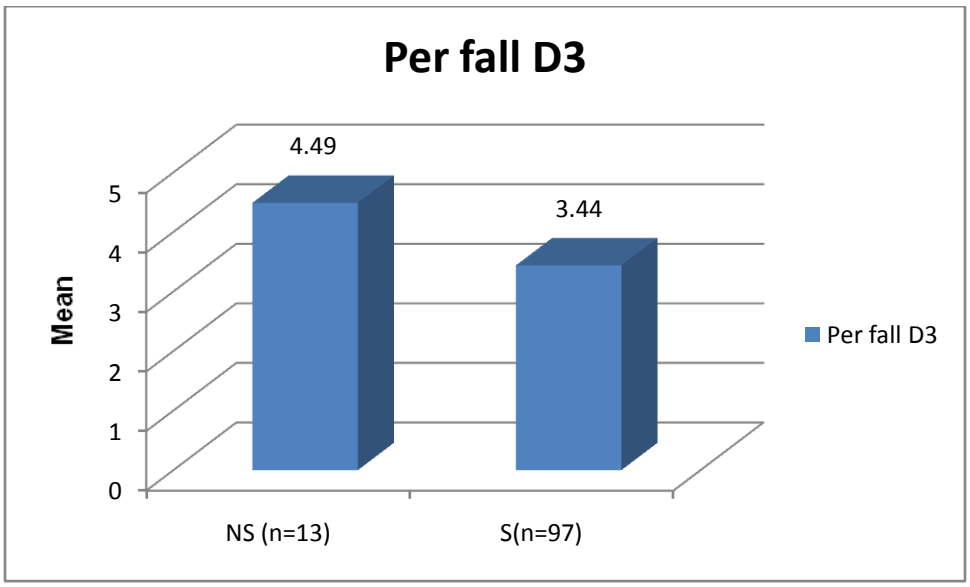

FIGURE 22: PERCENTAGE FALL IN SERUM ALBUMIN DAY 3 VS PATIENT SURVIVAL

TABLE 23: PERCENTAGE FALL IN SERUM ALBUMIN DAY 7 VS PATIENT SURVIVAL

	NS (n=13)		S(n=97)		t	p-value
	Mean	SD	Mean	SD		
Per fall D7	8.16	3.29	6.38	2.76	2.123	0.036

Table shows percentage fall in serum albumin at day 7 of the study with respect to patient survival

Among the patients who did not survive (13 patients), the mean percentage fall in serum albumin by Day 7 was found to be 8.16% with SD of 3.29 %. The group with patients who survived showed a percentage fall in serum albumin of 6.38% with SD of 2.76%.

Percentage fall in serum albumin by day 7 was found to be significantly higher among non survivors. (p value<0.05) in comparison to survivors.

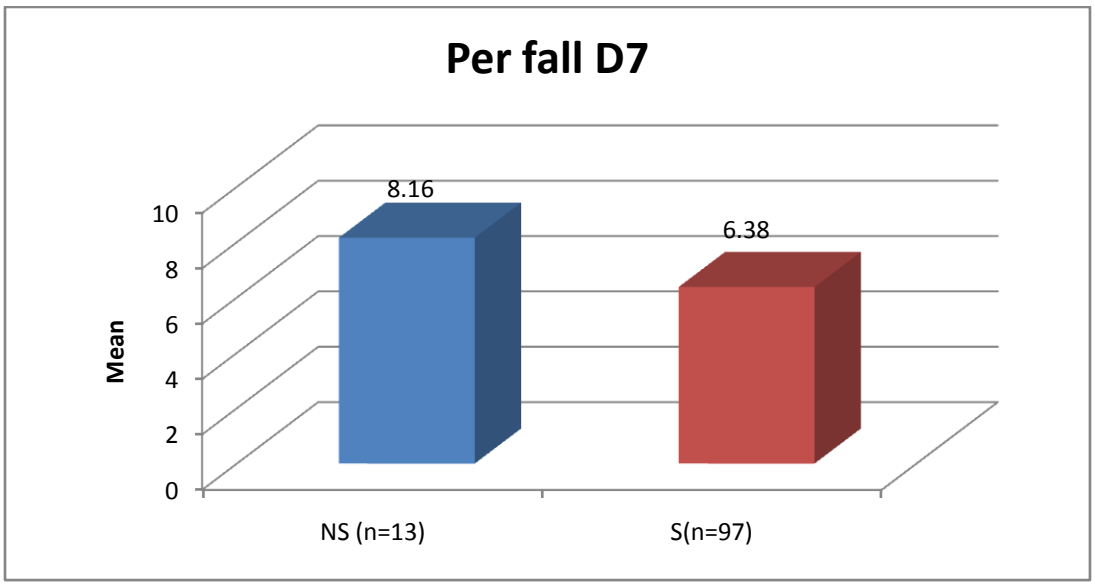

FIGURE 23: PERCENTAGE FALL IN SERUM ALBUMIN DAY 7 VS PATIENT SURVIVAL

TABLE 24: PERCENTAGE FALL IN SERUM ALBUMIN DAY 10 VS PATIENT SURVIVAL

	NS (n=13)		S(n=97)		t	p-value
	Mean	SD	Mean	SD		
Per fall D10	12.46	3.05	9.48	3.73	2.761	0.007

Tableshows percentage fall in serum albumin at day 10 of the study with respect to patient survival

Among the patients who did not survive (13 patients), the mean percentage fall in serum albumin by Day 10 was found to be 12.46% with SD of 3.05 %. The group with patients who survived showed a percentage fall in serum albumin of 9.48% with SD of 3.73%.

Percentage fall in serum albumin by day 10 was found to be significantly higher among non survivors. (p value<0.05) in comparison to survivors.

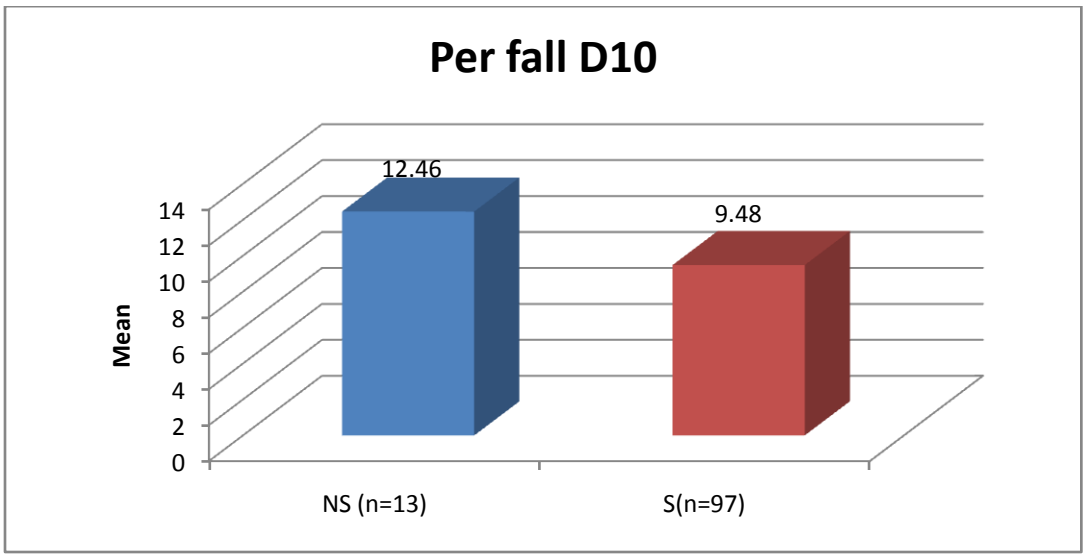

FIGURE 24: PERCENTAGE FALL IN SERUM ALBUMIN DAY 10 VS PATIENT SURVIVAL

TABLE 25.1: MEAN SERUM ALBUMIN VS PATIENT MANAGEMENT

		Management				Total	Chi-square value	p-value
		Conservative[C] (n=39)		Surgical[Su] (n=71)				
S.ALB D1 GROUP	Hypoa	17	43.6%	52	73.2%	69	9.465	0.002
	Normal	22	56.4%	19	26.8%	41		

Table showing analysis of mean serum albumin vs patient management.

Among the total 110 patients studied 39 (35.5%) patients were managed conservatively and 71 (64.5%) were managed with surgical intervention. In the patients managed conservatively 17 (43.6%) had hypoalbuminemia and 22 (56.4%) patients had normal serum albumin levels. In the 71 patients managed with surgical intervention 52 (73.2%) patients had hypoalbuminemia and 19 (26.8%) patients had normal mean serum albumin level

On statistical analysis mean serum albumin was significantly lower in surgical group as compared to conservative group p value 0.002.

C- Conservative
Su- surgical intervention

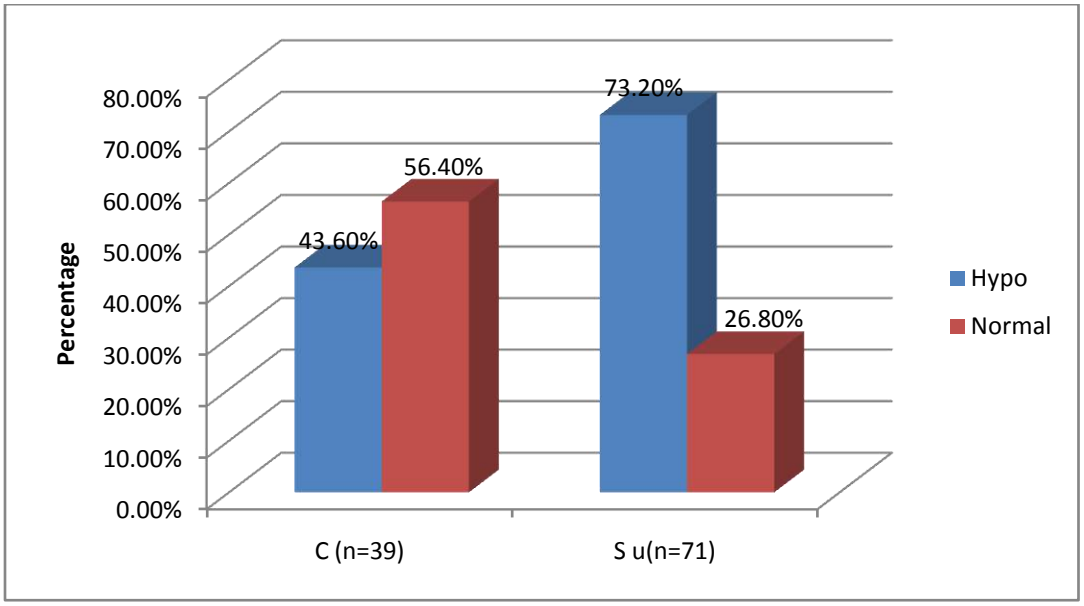

FIGURE 25.1: MEAN SERUM ALBUMIN VS PATIENT MANAGEMENT

TABLE 25.2: MEAN SERUM ALBUMIN IN CONSERVATIVE AND SURGICAL GROUPS

Management	Conservative (n=39)		Surgical (n=71)		t	p-value
S.ALB D1	Mean	SD	Mean	SD		
Mean	3.49	0.10	3.43	0.09	3.374	0.001
Median	3.50		3.41			
Min-Max	3-4.0		3-4.0			

Table showing mean levels of serum albumin in patients managed conservatively and those managed with surgical intervention

In the conservative group mean level of serum albumin was 3.49 g/dl with SD of 0.1, with a mean value of 3.5 g/dl. In the surgically treated group the mean value of serum albumin was 3.43 g/dl with SD of 0.09 and mean value of 3.41g/dl. On statistical analysis mean serum albumin was significantly lower in surgical group as compared to conservative group p value 0.001.

C- Conservative

Su- Surgical

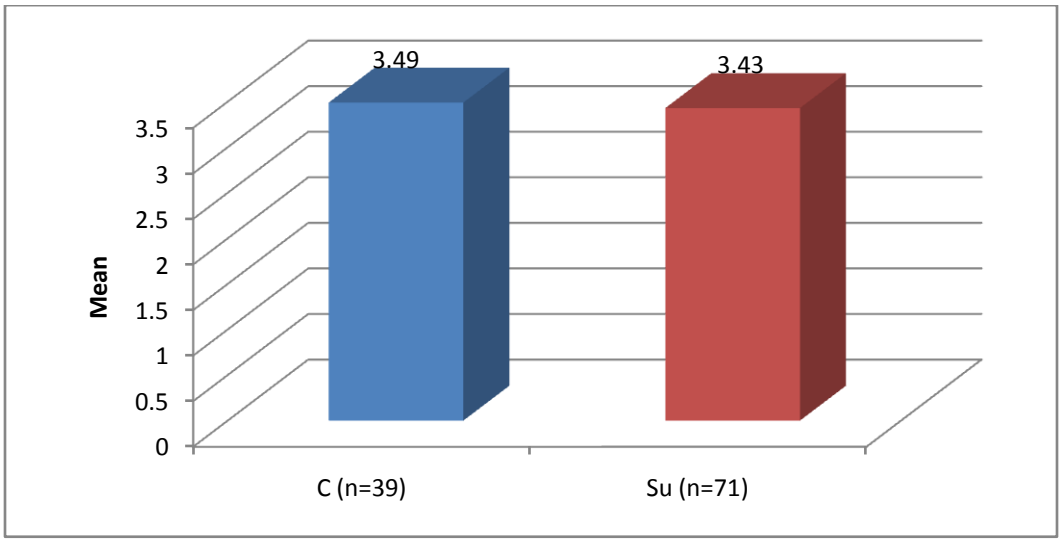

FIGURE 25.2: MEAN SERUM ALBUMIN IN CONSERVATIVE AND SURGICAL GROUPS

TABLE 26: MEAN SERUM ALBUMIN VS DURATION OF HOSPITAL STAY

	Hypoalbuminemia (n=69)		Normalbuminemia (n=41)		t	p-value
DAYS OF HOSPITAL STAY	Mean	SD	Mean	SD		
Mean	17.03	2.561	14.10	1.855	6.395	0.000
Median	17.00		14.00			
Min-Max	10	24	10	18		

Table shows comparison of mean serum albumin vs duration of hospital stay in days

In our study the patients having serum albumin levels < 3.5 g/dl (hypoalbuminemia) group, mean duration of hospital stay was 17.03 days with SD of 2.56 days with median of 17 days and min- max interval of 10-24 days. Among the patients with normal mean serum albumin mean duration of hospital stay was 14.10 days with SD of 1.85 days and min-max interval of 10-18 days.

On statistical analysis the correlation between mean serum albumin and hospital stay was found to be statistically significant (p<0.001).

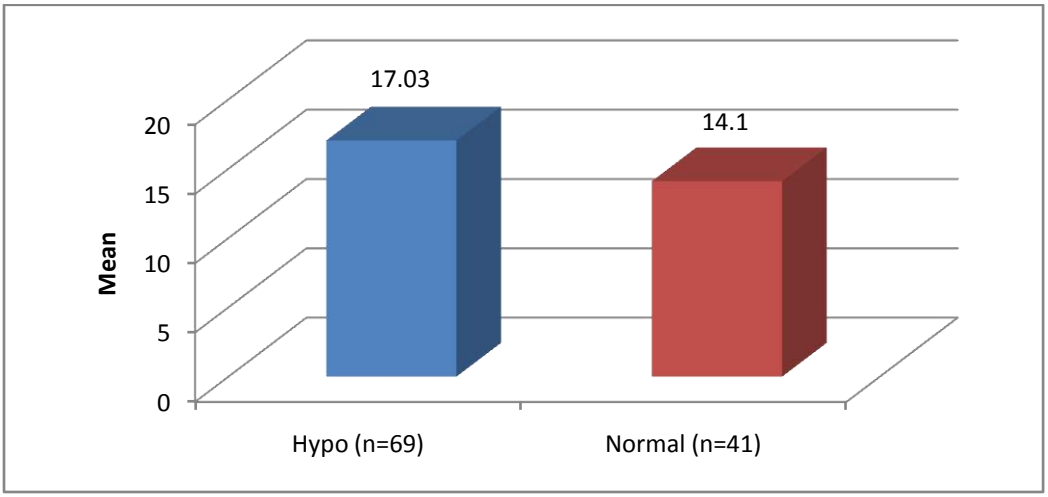

FIGURE 26: MEAN SERUM ALBUMIN VS DURATION OF HOSPITAL STAY

TABLE 27: MEAN SERUM ALBUMIN VS ICU STAY IN DAYS

	Hypo (n=69)		Normal(n=41)		t	p-value
ICU STAY DAYS	Mean	SD	Mean	SD		
Mean	6.94	1.533	5.56	1.246	4.886	0.000
Median	7.00		6.00			
Min-Max	4	11	3	8		

Table shows comparison of mean serum albumin vs ICU stay in days

In our study the patients having serum albumin levels < 3.5 g/dl (hypoalbuminemia) group, mean duration of ICU stay was 6.94 days with SD of 1.53 days with median of 7 days and min- max interval of 4-11 days. Among the patients with normal mean serum albumin mean duration of ICU stay was 5.56 days with SD of 1.246 days and min-max interval of 3-8 days.

On statistical analysis the correlation between mean serum albumin and ICU stay was found to be statistically significant (p<0.001).

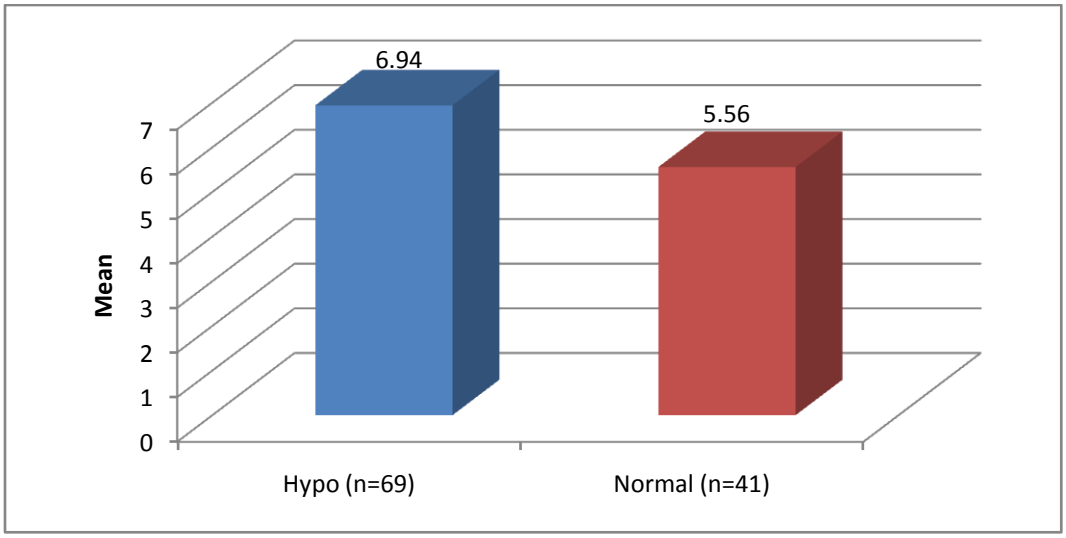

FIGURE 27: MEAN SERUM ALBUMIN VS ICU STAY IN DAYS

TABLE 28: MEAN SERUM ALBUMIN VS DAYS OF MECHANICAL VENTILATION

	Hypoalbuminemia (n=69)		Normalbuminemia (n=41)		t	p-value
VENTILATORY SUPPORT DAYS	Mean	SD	Mean	SD		
Mean	5.17	1.361	4.00	1.025	4.774	0.000
Median	5.00		4.00			
Min-Max	2	8	2	6		

Table shows comparison of mean serum albumin vs days of mechanical ventilation

In our study the patients having serum albumin levels < 3.5 g/dl (hypoalbuminemia) group, mean duration of mechanical ventilationwas 5.17 days with SD of 1.36 days with median of 5 days and min- max interval of 2-8 days. Among the patients with normal mean serum albumin mean duration of mechanical ventilation was 4 days with SD of 1.025 days and min-max interval of 2-6 days.

On statistical analysis the correlation between mean serum albumin and duration of mechanical ventilation was found to be statistically significant ($p<0.001$).

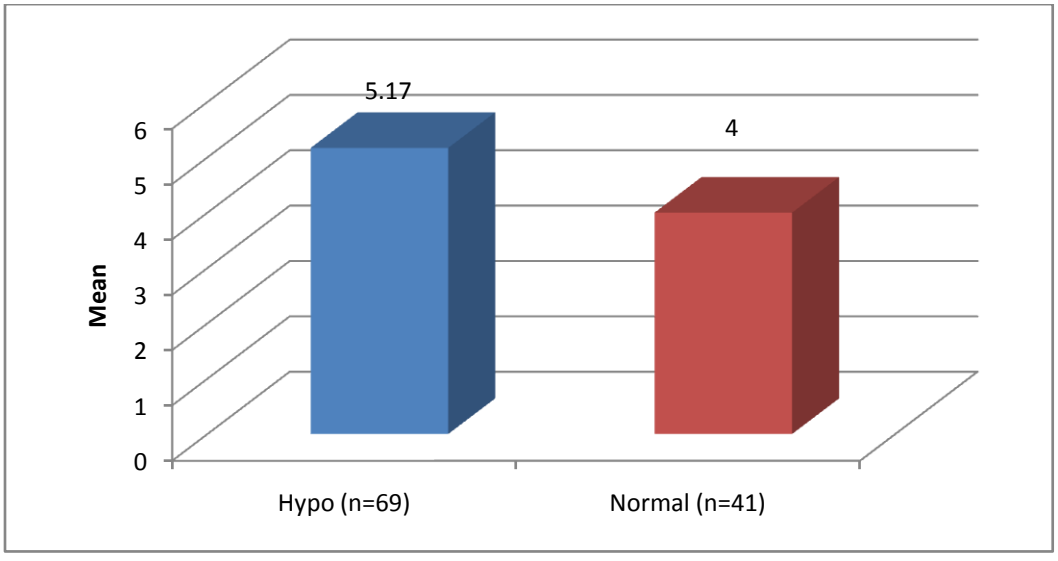

FIGURE 28: MEAN SERUM ALBUMIN VS DAYS OF MECHANICAL VENTILATION

TABLE 29.1: MEAN SERUM ALBUMIN VS COMPLICATIONS

		COMPLICATION				Total	Chi-square value	p-value
		No (n=77)		Yes (n=33)				
S.ALB D1 GROUP	Hypo	43	55.8%	26	78.8%	69	5.201	0.023
	Normal	34	44.2%	7	21.2%	41		

Table shows comparison of mean serum albumin vs complications

In our study out of total 110 patients, 33 patients had complications and 77 patients had no complications. Out of the 33 patients having complications, 26 patients (78.8%) had low mean serum albumin and 7 patients (21.2%) patients had normal value of serum albumin. In the 77 patients having no complications 43 patients (55.8%) had hypoalbuminemia and 34 patients (44.2%) patients had normalbuminemia. On statistical analysis the percentage of patients with hypoalbuminemia had higher complication rate as compared to the patients having normal serum albumin, p value 0.023.

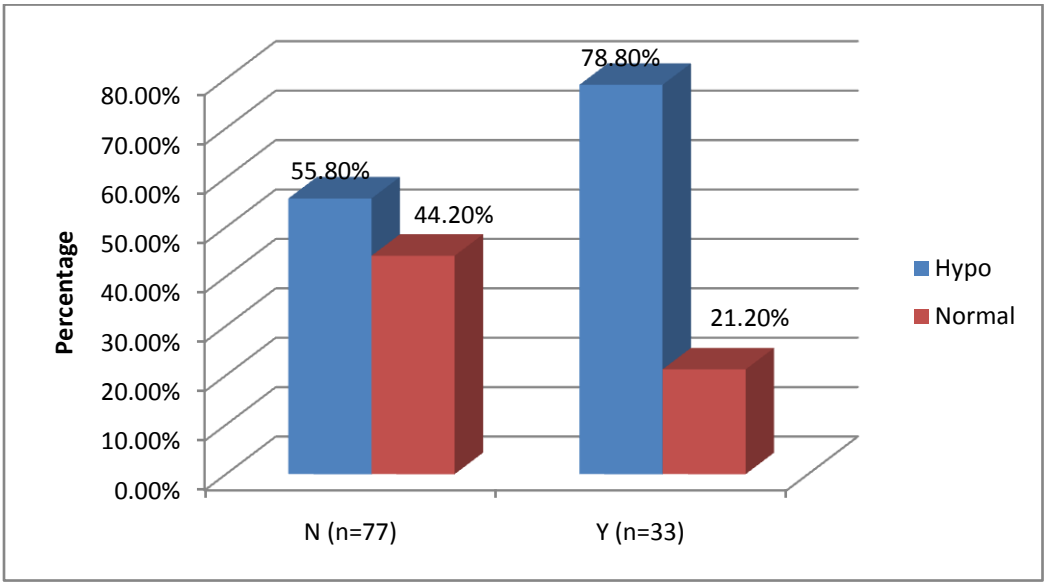

FIGURE 29.1: MEAN SERUM ALBUMIN VS COMPLICATIONS

TABLE 29.2: MEAN SERUM ALBUMIN VS COMPLICATIONS

		SA-MEAN			
		1)Normal (n=41)	2)Hypo albuminemia (n=69)	Total	P value
COMPLICATIONS	Y	7 (17.07%)	26(37.68%)	33	
	N	34(82.9%)	43(62.31%)	77	0.025
Total		41	69		

Table shows rate of complications in patients having hypoalbuminemia and normalbuminemia

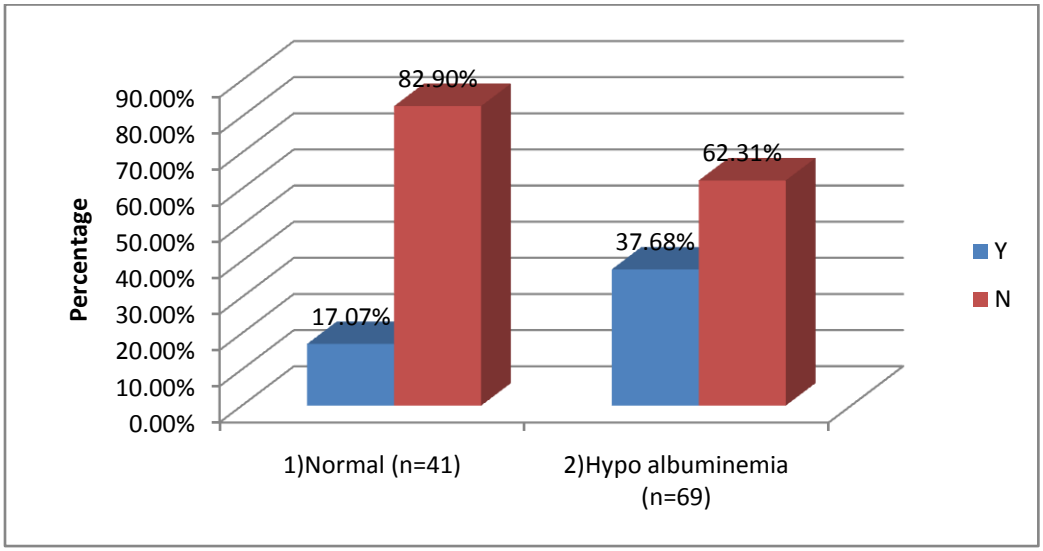

FIGURE 29.2: MEAN SERUM ALBUMIN VS COMPLICATIONS

TABLE 29.3: OUTCOME VS COMPLICATIONS

		OUTCOME GOS ON DISCHARGE(F/UF)				Total	Chi-square value	p-value
		F (n=32)		UF (n=78)				
Complications	No	29	90.6%	48	61.5%	77	9.141	0.003
	Yes	3	9.4%	30	38.5%	33		

Table shows rate of complications in favorable and unfavorable outcome groups

In our study 38.5% of patients with unfavorable outcome had complications whereas only 9.4% of patients having favorable outcome had complications, the difference was found to be statistically significant p value 0

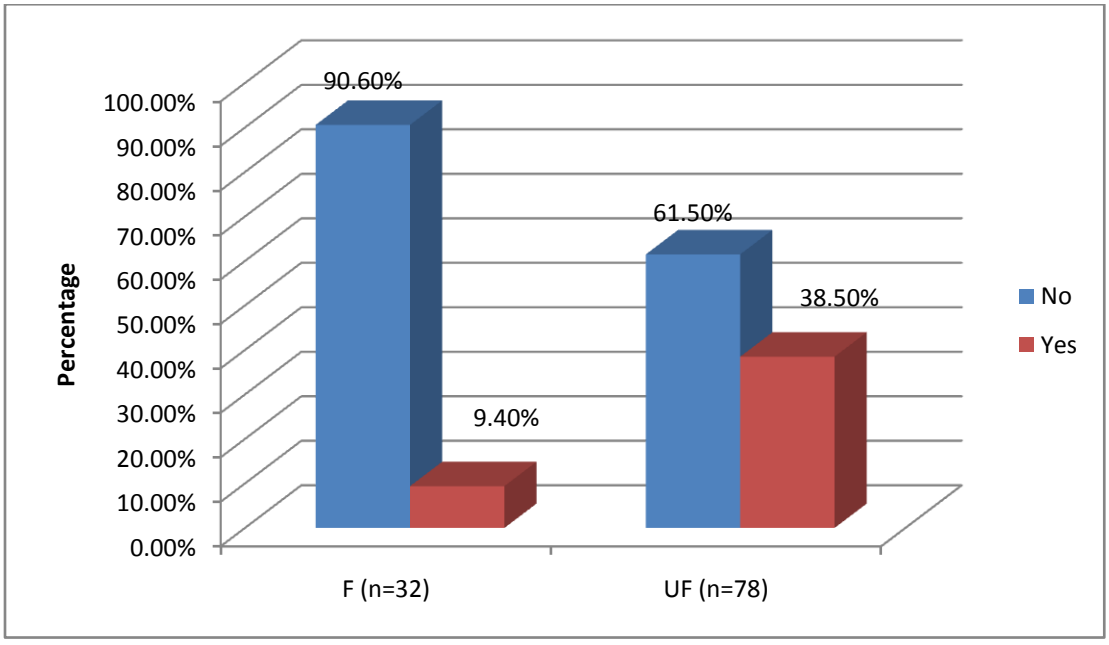

TABLE 29.3: MEAN SERUM ALBUMIN VS COMPLICATIONS

DISCUSSION

Severe traumatic brain injuries are catastrophic injuries primarily afflicting young individuals. Mortality ranges from 30% to 50%, while 30% of survivors suffer from severe neurological squeal. Given the majority of victims are young with previous excellent quality of life, substantive human, social and financial repercussions are experienced by survivors. Assessing long-term neurological outcome after such injury is difficult and often characterized by uncertainty.[11] With regard to victims of severe traumatic brain injury, physicians and families often face important treatment decisions. They must decide to either undertake aggressivecare in the hope that the patient will survive with an acceptable quality of life,[93-96]or to withdraw lifesustaining therapies considering an unfavorable and undesirable prognosis. Serious concerns have been expressed regarding early decisions made to withdraw life-sustaining therapies in the absence of evidencebased prognostic information.[97-100]

Serum albumin level is correlated with outcome in various clinical situations. Albumin has multiple physiologic properties that could be beneficial in brain injury. The Lund therapy for elevated intracranial pressure uses albumin as part of its protocol and demonstrates favorable outcome.[90] The objective of this study was to analyze the role of serum albumin as a predictor of prognosis and outcome in cases of severe traumatic brain injury.

In our study a total of 110 patients falling within the age group of 18-65 years having severe traumatic brain injury (GCS≤8) were studied. Patients with preexisting medical conditions were excluded. Out of total 110 patients majority of patients were in 3rd ,4th and 5th decade of life, maximum between 31-40 year age group bracket, minimum number of patients were the ones below 20 years of age.

Dhandapani et al[89] in 2005 studied 67 patients with severe traumatic brain injury, in this study the mean age of study sample was 35.4 years. In a study by Rajendran et al[23] out of 54 patients studied the majority of

population was between 30-50 years. Pandey et al[92] conducted a study in which 200 patients including 50 controls of traumatic brain injury were analyzed. The incidence of traumatic brain injury was found to be more in 3rd and 4th decade.

In our study out of 110 patients, 25(22.7%) were female and 85(77.3%) were male, roughly equating to ratio of 1:3.4 In study by Dhandapani et al[89] out of 67 patients studied 62 were male and 5 were female. In study by Rajendran et al[23] out of 54 patients studied, 49(90.7%) were male and only 5(9.3%) patients were female. Pandey et al[92] also reported majority of patients being male with male to female ratio being 3.1:1. This increased incidence of head injury among males in comparison to females can be attributed to behavioral and lifestyle differences resulting in a difference in exposure to trauma.

Several studies over the years have established various causes of head injury. Road traffic accident is usually the commonest cause of head injury in both developed and developing nations. In our study, 68.2% patients were injured during a road traffic accident, making it the commonest cause. The remaining patients were either reported to have fallen from a height (21.8%) or were allegedly assaulted (10%).

In our study, 33.6% patients were found to have Subdural hematoma, and 26.4% patients had hemorrhagic contusion. Intracerebral hemorrhage was found in 7.3% patients of severe head injury. Extradural hematoma was also found in only 5.5 % of these patents. 27.3% patients had other miscellaneous diagnosis. In study by Pandey et al[92] majority of the patients had contusions (28%) and multiple intra cerebral hemorrhages (28%) followed by equal number of patients with diagnosis of SDH (12.5%) and EDH (12.5%).

All of our patients had severe traumatic brain injury GCS≤8. In studies by Dhandapani et al[89] patients with moderate head injuries were included as well. Bernard F et al[90], Pandey et al[92] and Rajendran et al[23] included all the patients of mild, moderate and severe head injury.

In our study we assessed the outcome of patient in discharge and classified them into having favorable and unfavorable outcome.GOS Grade 1, 2, 3 was taken as unfavorable outcome and GOS Grade 4 and 5 was taken as favorable outcome. Dhandapani et al[89],Pandey et al[92] and Bernard F et al[90 also used the Glasgow outcome Scale to evaluate patient outcome. They had however evaluated the patient outcome till 6 months after discharge of the patient.

In our study, we measured Total Serum Protein levels within 24 hours of admission and Serum albumin levels within 24 hours of admission and on Day 3, Day 7 and Day 10.Pandey et al[92] measure Serum albumin within 24 hours of admission and on day 3, day5, day10. Dhandapani et al[34] and Bernard F et al[90] recorded serum albumin up to Day 21.

We, in our study have considered mean serum Albumin levels less than 3.5 g/dL as hypoalbuminemia.

In our study, out of 110 patients, 78 patients (70.9%) had unfavorable outcome at discharge, and 32 patients (29.1%) patients had unfavorable outcome. Bernard F et al[90] had a favorable outcome in 70% of their patients and 30% of their patients had an unfavorable outcome at 6 months. Dhandapani et al[89] noted unfavorable outcome at 3 months in 62% patients having hypoalbuminemia at admission, in comparison to 18% of those having normal levels (p value < 0.001). Pandey et al[92] in their study also noted similar findings, where 76% of the patient having unfavorable outcome had hypoalbuminemia and only 32% of the favorable group had hypoalbuminemia.Du Chen et[26] in their study demonstrated, in patients of TBI with serum albumin ≥3.5 g/dl, the proportion of unfavorable outcome was reduced significantly

In our study out of 78 patients having unfavorable outcome, 61 patients (78.2%) had hypoalbuminemia and 17 patients (21.8%) had normal albumin levels at time of admission (D1). 32 patients hadfavorable outcome, out of these 24 patients (75%) had normal albumin levels and 8 patients (25%) had hypoalbuminemia.

There was a statistically significant correlation between hypoalbuminemia and unfavorable patient outcome Mean serum albumin on admission was significantly higher in group with favorable outcome i.e 3.54 with standard deviation of 0.08 as compared to group with unfavorable outcome ie 3.42 with standard deviation of 0.08. This difference was found to be statistically significant with a p value < 0.001.

We also compared the percentage fall in mean serum albumin by Day 3, Day 7 and Day 10. Significant fall in mean serum albumin was noted on day 10, 9.8% with standard deviation of 3.8%. In our study we also analyzed the correlation of percentage fall in serum albumin in favorable and unfavorable groups of outcome.

Among the 32 patients with favorable outcome the percentage fall in serum albumin at day 3 was 2.24% with standard deviation of 1.12%. In the unfavorable group the percentage fall in serum albumin was 4.02% with standard deviation of 1.78. At day 7 percentage fall in serum albumin in 32 patients with favorable outcome was 4.3% with standard deviation of 1.19%. In the unfavorable group the percentage fall in serum albumin was 7.53% with standard deviation of 2.83%. At day 10 percentage fall in serum albumin in 32 patients with favorable outcome was 6.06 % with standard deviation of 1.45 %. In the unfavorable group the percentage fall in serum albumin was 11.37% with standard deviation of 3.32%.

Dhandapani et al[34] compared the patient outcome versus the percentage fall in serum albumin by 3 weeks of admission. The unfavorable outcome was noted in 12 out of 15 patients with at least 15% fall in serum albumin levels at 3 weeks as compared to 11 out of 25 patients with less than 15% fall in serum albumin and the difference was statistically significant. In Bernard F et al[90] study, albumin levels were higher in the first few days after injury in patients with a good outcome.The albumin levels decreased appreciably compared with normal values in both groups. However, the albumin levels remained below 2.5 g/dL for a longer period of time in the group with a poor outcome.Pandey et al[92] in their study demonstrated fall

in serum albumin was 18.65% from day1to day10 in unfavorable group comparing to 8.63% in favorable group.Correlating with above studies from literature and the findings of our study we can conclude that fall in serum albumin over the course of treatment has a direct impact on outcome of the patient.

Different studies have correlated the severity of head injury to the outcome, in our study we only took cases of severe traumatic brain injuries

We also studied impact of age and gender on the outcome but we didn't find any statistically significant correlation. P values of 0.792 and 0.716 for age and gender respectively. In the study of Dhandapani et al[89], age more than 40 years, admission GCS less than 9 and admission serum albumin less than 3.5 g/dL emerged as independent predictors for unfavorable outcome at 3 months. Bernard F et al[90] study showed no correlation between age, gender and outcome. Pandey et al[92] showed that female TBI patients have less no. of hypoalbuminemia compared to male as 77.7%, 45.4%, 31.4% male and 42.8%, 28.5%, 27.2% female having hypoalbuminemia (< 3.5 gm/dl) in severe, moderate and mild head injury respectively and statistically significant difference in severe and moderate group.

In our study we tried to study correlation between mode of injury and outcome, no significant correlation was present between mode of injury and outcome p value 0.860. Similarly we also analyzed from the data that diagnosis code also didn't have impact on patients outcome p value 0.873. This suggests, that mode of injury and diagnosis code may not be a reliable or independent predictor of patient outcome.

Out of the total 110 patients studied 13 patients (11.8%) expired during the course of treatment,97 patients (88.2%) survived. Out of 97 patients who survived 56 (57.7%) had hypoalbuminemia and 41 (42.3%) patients had normal level of serum albumin at the time of admission. All the non survival group patients had hypoalbuminemia. Mean serum albumin level

on admission of survival group was 3.47 g/dl with standard deviation of 0.09 and that of non survival group was 3.37 g/dl with standard deviation of 0.06.On statistical analysis significant correlation was found between survival and admission level of serum albumin with p value of 0.002.

In our study we also compared percentage fall in serum albumin at day 3, day 7 and day 10 with survival. Among the patients who did not survive (13 patients), the mean percentage fall in serum albumin by Day 3 was found to be 4.49 ± 1.36 %. The group with patients who survived showed a percentage fall in serum albumin of 3.34 ± 1.78%. The mean percentage fall in serum albumin by Day 7 was found to be 8.16± 3.29 % in non survival group. The group with patients who survived showed a percentage fall in serum albumin of 6.38 ± 2.76%. At day 10 of the study the percentage fall in serum albumin in non survival group was found to be 12.46± 3.05 %. The group with patients who survived showed a percentage fall in serum albumin of 9.48 ± 3.73%. Upon statistical analysis the percentage fall of serum albumin was significantly higher in non survival group as compared to those who survived.

Dhandapani et al[89] also compared the serum albumin levels with patient survival. They found that 43% patients with hypoalbuminemia had expired as compared to 17% of those with acceptable serum albumin levelsat 1 month and significant increase in mortality at 2 months among patients with at least 15% fall in serum albumin and urinary creatinine less than 1000mg/dl at 3 weeks. In Rajendran et al[23] study Patients with serum albumin ≥ 3.5 g/dL showed a significantly higher chance to survive than patients with hypoalbuminemia. The progression – free survival rate was significantly worse in the hypoalbuminemia group (log-rank test, $p < 0.001$). In Yap FH et al,[101] study survivors had higher admission albumin (2.57 g/dl vs 2.10 g/dl, $p<0.005$) than non survivors.

Pandey et al[92] also studied this correlation, in their study mean serum albumin level on day of admission (Day 1) for the study group was 3.76 g/dl (± 0.4 gm/dl) and in survivors, it was 3.81 gm/dl (± 0.3 gm/dl) and

highly significantly lower ($p < 0.001$) in non survivors 3.35 g/dl (± 0.6 g/dl). In the survivor group, 62.71% patients have normal serum albumin levels on admission as compared to just 8.75% in the non survivor group, suggesting hypoalbuminemia at admission indicates a poorer prognosis in terms of increased mortality. McCluskey A et al[102] in their study also reported that nonsurvivors had lower serum albumin concentrations on admission to the ICU, and their albumin concentrations decreased more rapidly in the first 24 to 48 h.

These studies correlate with our study findings, so it can be said that low mean admission levels of serum albumin can be associated with low chance of survival.

In our study, we divided our patients into two groups i.e. patients with normal serum albumin levels and patients with hypoalbuminemia. These two groups were then compared in terms of duration of hospital stay, duration of ICU stay and duration of Mechanical ventilation.

In our study the patients having serum albumin levels < 3.5 gm/dl (hypoalbuminemia) group, mean duration of hospital stay was 17.03 days with standard deviation of 2.56 days with median of 17 days and min- max interval of 10-24 days. Among the patients with normal mean serum albumin mean duration of hospital stay was 14.10 days with standard deviation of 1.85 days and min-max interval of 10-18 days. On statistical analysis the correlation between mean serum albumin and hospital stay was found to be statistically significant ($p<0.001$).

With respect to days of ICU stay, in our study the patients having serum albumin levels < 3.5 gm/dl (hypoalbuminemia) group, mean duration of ICU stay was 6.94 days with standard deviation of 1.53 days with median of 7 days and min- max interval of 4-11 days. Among the patients with normal mean serum albumin mean duration of ICU stay was 5.56 days with standard deviation of 1.246 days and min-max interval of 3-8 days. On statistical analysis the correlation between mean serum albumin and ICU stay was found to be statistically significant ($p<0.001$).

Bernard F et al[90], in their study reported that the patients of the favorable group spend an average of 7 days in the ICU as compared to 11 days spent by the unfavorable group. Moreover, they observed that hypoalbuminemia was more sustained among the patients who spent more time in the Critical care unit. In the study by Pandey et al mean duration of Neuro ICU stay was 8.08 (±3.008) days and 3.84 (±2.433) days in group of albumin less than 3.5 g/dl and more than 3.5 gm/dl respectively and difference was statistically significant (p<0.001).

In our study the patients having serum albumin levels < 3.5 g/dl (hypoalbuminemia) group, mean duration of mechanical ventilation was 5.17 days with standard deviation of 1.36 days with median of 5 days and min- max interval of 2-8 days. Among the patients with normal mean serum albumin mean duration of mechanical ventilation was 4 days with standard deviation of 1.025 days and min-max interval of 2-6 days.On statistical analysis the correlation between mean serum albumin and duration of mechanical ventilation was found to be statistically significant (p<0.001).

Bernard F et al[90] in their study reported that the patients in the favorable group spent an average of 4 days and the unfavorable group spent an average of 9 days on mechanical ventilation (p value < 0.001). The mean duration of mechanical ventilation was significantly higher among patients with hypoalbuminemia in comparison to patients with normal levels. Pandey et al[92] reported statistically significant (p=0.011) difference in the mean duration of mechanical ventilation was observed between group of hypoalbuminemia and normoalbuminemia 5.92 (±3.008) days and 3.50 (±2.433) respectively.

Thus in respect to predicting the days of hospital stay, ICU stay and mechanical ventilation results of our study are comparable to the above studies. It can therefore be inferred that hypoalbuminemia can be a useful predictor of hospital stay, mechanical ventilation and ICU stay and help the hospital to manage its critical care resourced more efficiently.

Hypoalbuminemia has been associated with increased propensity for complications like surgical site infections, respiratory tract infections, urinary tract infections, wound dehiscence and CSF leak. Hypoalbuminemia has also been associated with systemic complications like cardiac, hepatic, renal etc. In our study 37.68% of the patients with hupoalbuminemia had complications whereas 17.07% patients with normal serum albumin had complications, rate of complication was significantly higher in hypoalbuminemia group with p value 0.0225. In our study 38.5% of patients with unfavorable outcome had complications whereas only 9.4% of patients having favorable outcome had complications, the difference was found to be statistically significant p value 0.003.

Pandey et al[92] in their study showed that the complications like infection, delayed wound healing was higher for unfavorable group (14.9%) than in favorable group (8.5%), although the difference was statically insignificant (p=0.201)

In our study Out of the total 110 patients 71 patients (64.5%) were managed with one or more surgical procedure, 39 patients (35.5%) patients were managed conservatively. In the conservative group mean level of serum albumin was 3.49 g/dl with standard deviation of 0.1, In the surgically treated group the mean value of serum albumin was 3.43 g/dl with standard deviation of 0.09 which was significantly lower p value (0.001) . In the patients managed conservatively 17 (43.6%) had hypoalbuminemia and 22 (56.4%) patients had normal serum albumin levels. In the 71 patients managed with surgical intervention 52 (73.2%) patients had hypoalbuminemia and 19 (26.8%) patients had normal mean serum albumin level. On statistical analysis mean serum albumin was significantly lower in surgical group as compared to conservative group p value 0.002.

Dhandapani et al[34] in their study noted that 36% of patients undergoing surgical management had hypoalbuminemia with serum albumin fall ≥15%

at 3 weeks as compared to 25 % patients in non surgical group. In another study by the same authors also observed that patients who required surgical decompression were found to have significantly lower serum albumin levels (mean 3.15 ± 0.5 g/dL) compared to those having no surgically remediable lesion (mean 3.35 ± 0.5 g/dL) ($p = 0.02$)

Surgery is in itself stressful condition which brings about plethora of physiological and biochemical changes in the body. A number of pre and perioperative interventions can be done to decrease the surgical stress in order to have positive outcome. In our study we have shown that this can be achieved by identifying such patients which are more prone to surgical stress with help of simple and economical test that is serum albumin estimation. The strong correlation between hypoalbuminemia and increased incidence of surgical management in patients of TBI suggests that Serum Albumin levels can be used as an effective prognostic indicator in these patients.

Very few biomarkers of the severity of head injury are clinically available, it is imperative to study each in relation to neurological outcome. Serum albumin plays a wide variety of roles. It is the chief determinant of plasma oncotic pressure. It has antioxidant property. The prognostic significance of serum albumin stems from its merit of being a marker of nutritional status too besides its immune modulatory properties. Traumatic brain injury is also an acute condition, where outcome prediction is impeded by a reliable marker. Hence in our study we explored the possibility of using serum albumin to predict the poor outcome in TBI which is a stressful condition.

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SUMMARY AND CONCLUSION

Head injury is a major cause of morbidity and mortality in society, particularly the young adults. Even in case of patients survival it is associated with sequel of physical disability, long term cognitive and psychological damage. It is important for doctors to prognosticate patient of TBI early in the course of treatment so as to predict the outcome of patient in future. It is also important for efficient and judicious use of healthcare infrastructure.

We conducted our study to elucidate the role of serum Albumin as a prognostic marker in severe traumatic brain injury. 110 patients with severe head injury (GCS ≤ 8) admitted in the emergency and trauma center of DAYANAND MEDICAL COLLEGE AND HOSPITAL LUDHIANA. The study was conducted under Department of Neurosurgery.

Following factors were recorded for each patient during the course of treatment of the patient:-

1. HISTORY AND EXAMINATION:- history, mode of injury ,general examination, GCS, and pupillary reaction were recorded
2. RADIOLOGY:- Each patient underwent plain CT head based on which diagnosis was made and management decided
3. BIOCHEMISTRY:- Patients underwent routine blood investigations along with which serum albumin was noted first in the day of admission then at 3^{rd}, 7^{th} and 10^{th} day of the patients course of treatment.
4. MANAGEMENT:- Patient management was decided based on diagnosis, accordingly patients were managed conservatively or surgically, patients were kept in ICU and Ventilatory support was provided according to requirement.
5. DURATION:- Duration of stay of the patient in ICU, on Mechanical ventilation and hospital was recorded.
6. COMPLICATIONS:- Complications like respiratory tract and urinary tract infections, surgical site infection, CSF leaks were noted

7. OUTCOME:- patient outcome was decided at discharge based on Glasgow Outcome Score

The data so collected was subjected to statistical analysis and following observations were made

1. Patients with unfavorable outcome had lower mean serum albumin at time of admission
2. Patient with normal serum albumin had better chance of survival as compared to those with low serum albumin at time of admission
3. Percentage fall in mean serum albumin significantly correlates with unfavorable outcome
4. Patients with more percentage fall in serum albumin were less likely to survive
5. Patients with low serum albumin at time of admission had more days of mechanical ventilation, more days of ICU stay and more stay at hospital
6. Proportion of patients with hypoalbuminemia was relatively higher in surgically managed patients as compared to conservatively managed patients
7. Proportion of patients with complications were relatively higher in those who had low serum albumin at time of admission

This study was our sincere attempt to explore the possibility of an economical and common biomarker to prognosticate the patients with severe traumatic brain injury. At the end we can conclude that serum albumin can be employed as an effective indicator and prognostic tool for determination of outcome in patients with severe traumatic brain injury.

BIBLIOGRAPHY

1 Salehpoor F, Meshkini A, ShokouhiGh, Aghazade J, Lotfinia I, Shakeri M, et al. Prognostic Serum Factors in. Traumatic Brian Injury: A Systematic Review. Iran J Neurosurg. 2015;1(1):10-22.

2 Barlow P, Teasdale G. Prediction of outcome and the management of severe head injuries: the attitudes of neurosurgeons. Neurosurg. 1986;19(6):989-91.

3 Chestnut R.M, GhajarJ ,Maas A , Marion D.W, Franco S, Teasdale G, et al.Early indicators of prognosis in severe traumatic brain injury. Journal of Neurotrauma.2000;7:555-627.

4 Puvanachandra P, Hyder AA. The Burden Of Traumatic Brain Injury In Asia: A Call For Research. Pak J NeurolSci. 2009; 4(1):27-32.

5 Shekhar C, Gupta LN, Premsagar IC, Sinha M, Kishore J. An epidemiological study of traumatic brain injury cases in a trauma centre of New Delhi (India). J Emerg Trauma Shock. 2015;8(3):131–9.

6 Finfer SR, Cohen J. Severe traumatic brain injury. Resuscitation. 2001;48(1):77-90.

7 Andreason F. Protein binding of drugs in plasma from patients with acute renal failure. ActaPharmacolToxicol. 1973;32(6):417–29.

8 Jennett B, Bono M. Assessment of outcome after severe brain damage. A practical scale. Lancet. 1975;305(7905):480-4.

9 Teasdale G, Jennet B. Assessment of coma and impaired consciousness. Lancet.1974;2:81-4.

10 Shahim P, Tegner Y, Wilson DH, Randall J, Skillbäck T, Pazooki D, et al. Blood biomarkers for brain injury in concussed professional ice hockey players. JAMA neurology. 2014;71(6):684-92.

11 Turgeon AF, Lauzier F, Zarychanski R, Fergusson DA, Léger C, McIntyre LA, et al. Prognostication in critically ill patients with severe traumatic brain injury: the TBI-Prognosis multicentre feasibility study. BMJ Open. 2017;7(4):e013779.

12 Papa L, Ramia MM, Edwards D, Johnson BD, Slobounov SM. Systematic review of clinical studies examining biomarkers of brain Injury in athletes after sports-related concussion. Journal of Neurotrauma. 2015;32(10):661–73.
13 Haqqani AS, Hutchison JS, Ward R, Stanimirovic DB. Protein biomarkers in serum of pediatric patients with severe traumatic brain injury identified by ICAT–LC-MS/MS. Journal of neurotrauma. 2007;24(1):54-74.
14 Apelgren KN, Rombeau JL, Twomey PL, Miller RA. Comparison of nutritional indices and outcomes in critically ill patients. Crit Care Med. 1982;10(5):305–7.
15 Berman RS, Frew JD, Martin W. Endotoxin-induced arterial endothelial barrier dysfunction assessed by an in vitro model. Br J Pharmacol. 1993;110(4):1282–4.
16 Bone RC. The pathogenesis of sepsis. Ann Intern Med. 1991;115(6):457-69.
17 Bradley JA, Cunningham KJ, Jackson VJ, Hamilton DN, Ledingham IM. Serum protein levels in critically ill surgical patients. Intensive Care Med. 1981;7(6):291-5.
18 Brenner DA, Buck M, Feitelberg SP, Chojkier M. Tumor necrosis factor-α inhibits albumin gene expression in a murine model of cachexia. J Clin Invest. 1990;85(1):248–55.
19 Brown RO, Bradley JE, Bekemeyer WB, Luther RW. Effect of albumin supplementation during parenteral nutrition on hospital morbidity. Crit Care Med. 1988;16(12):1177–82.
20 Blunt MC, Nicholson JP, Park GR. Serum albumin and colloid osmotic pressure in survivors and non-survivors of prolonged critical illness. Anaesthesia. 1998;53(8):755–61.
21 Boldt J, Heesen M, Mueller M, Pabsdorf M, Hempelmann G. The effects of albumin versus hydroxyethyl starch solution on

cardiorespiratory and circulatory variables in critically ill patients. AnesthAnalg. 1996;83(2):245–61.

22 Boldt J, Mueller M, Heesen M, Neumann K, Hempelmann G. Influence of different volume therapies and pentoxifylline infusion on circulating soluble adhesion molecules in critically ill patients. Crit Care Med. 1996;24(3):385–91.

23 Rajendran S, Govindan T, Vedavyasan M, Selvaraj K. Evaluation of serum albumin as a prognostic marker in traumatic brain injury. International Journal of Clinical Biochemistry and Research. 2017;4(3):299-304.

24 Burtis CA, Ashwood ER, Bruns DE. Teitz text book of clinical chemistry and molecular diagnosis. 2012;5:909.

25 KoertzenM, PunjabiPP, LockwoodGG. Pre-operative serum albumin concentration as a predictor of mortality and morbidity following cardiac surgery. Perfusion. 2013;28(5):390–4.

26 Du Chen LB, Lu SQ, Xu F. Serum albumin and prealbumin predict the poor outcome of traumatic brain injury. PLoS One. 2014;9(3):e93167.

27 Zhao Z-Y, Wu N, Deng SX, Zhou Y, Cao T-W. Serum albumin is a predictor for duration of weaning in patients with traumatic brain injury. Int J ClinExp Med. 2016;9(2):4041-6.

28 Fleck A, Hawker F, Wallace PI, Raines G, Trotter J, Ledingham IM, et al. Increased vascular permeability: a major cause of hypoalbuminaemia in disease and injury. Lancet. 1985;325(8432):781–4.

29 De Feo P, Horber FF, Haymond MW. Meal stimulation of albumin synthesis: a significant contributor to whole body protein synthesis in humans. Am J Physiol. 1992;263(4):E794–9.

30 Demling RH. Effect of plasma and interstitial protein content on tissue edema formation. Curr Stud Hematol Blood Transfusion. 1986;53:36–52.

31 Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systematic review of randomised controlled trials. Br Med J. 1998;317:235-40.

32 Cook D, Choi P. Review: albumin does not reduce death in critically ill patients with hypovolemia, burns, or hypoalbuminemia: Commentary. Evidence Based Med. 1999;4:19.

33 Mahapatra AK. Textbook of traumatic brain injury. JP publications. 2012;1:1-4.

34 Dhandapani SS, Manju D, Vivekanandhan S, Agarwal M, Mahapatra AK. Prospective longitudinal study of biochemical changes in critically ill patients with severe traumatic brain injury: Factors associated and outcome at 6 months. Indian Journal of Neurotrauma. 2010;7(01):23-8.

35 Peters T. All About Albumin. San Diego. Academic Press. 1995.

36 Fanali G, Di Masi A, Trezza V, Marino M, Fasano M, Ascenzi P. Human serum albumin: from bench to bedside. Mol Aspects Med. 2012, 33(3):209–90.

37 Vincent JL, Russell JA, Jacob M, Martin G, Guidet B, Wernerman J, et al. Albumin administration in the acutely ill: What is new and where next. Bio Med central. 2014;18:231.

38 Matejtschuk P, Dash CH, Gascoigne EW. Production of human albumin solution: a continually developing colloid. Br J Anaesth. 2000,85(6):887-95.

39 Klein S. The myth of serum albumin as a marker of nutritional status. Gastroenterology. 1990;99(6):1845–51.

40 Klonoff-Cohen H, Barrett-Connor EL, Edelstein SL. Albumin levels as a predictor of mortality in thehealthyelderly. J ClinEpidemiol. 1992;45(3):207-12.

41 Redman CM. Biosynthesis of serum proteins and ferritin by free and attached ribosomes of rat liver. Journal of Biological Chemistry. 1969;244(16):4308-15.

42 Pietrangelo A, Panduro A, Chowdhury JR, Shafritz DA. Albumin gene expression is down-regulated by albumin or macromolecule infusion in the rat. Journal of Clinical Investigation. 1992;89(6):1755–60.
43 Carter DC, Ho JX. Structure of serum albumin. Adv Protein Chem. 1994;45:153-203.
44 Kragh-Hansen U. Structure and ligand binding properties of human serum albumin. Danish Medical Bulletin. 1990;37(1):57–83.
45 Zachwieja JJ, Bier DM, Yarasheski KE. Growth hormone administration in older adults: effects on albumin synthesis. American Journal of Physiology. 1994;266(6):E840–4.
46 Hutson SM, Stinson-Fisher CA, Shiman RO, Jefferson LS. Regulation of albumin synthesis by hormones and amino acids in primary cultures of rat hepatocytes. American Journal of Physiology. 1987;252(3):E291-8.
47 Ganong WF. Dynamics of blood and lymph flow. In: Review of Medical Physiology. 1995;11:525–41.
48 Guyton AC & Hall JE. Human Physiology and Mechanisms of Disease. Philadelphia: WB Saunders. 1997;32:440-5.
49 Nicholson JP, Wolmarnas MR, Park GR. The role of albumin in critical illness. British journal of anesthesia. 2000;85:599-610.
50 Doweiko JP, Nompleggi DJ. Use of albumin as a volume expander. J Parent Enteral Nutr. 1991;15(4):484-7.
51 Hill PG. The measurement of albumin in serum and plasma. Annals Clinical Biochemistry. 1985;22(6):565–78.
52 Doweiko JP &Bistrian BR. The effect of glycosylated albumin on platelet aggregation. Journal of Parenteral and Enteral Nutrition. 1994;18(6):516–20.
53 Johnson TR, Rudin SD, Blossey BK, Ilan J. Newly synthesised RNA: simultaneous measurement in intact cells of transcription rates and RNA stability of insulin-like growth-factor 1, actin, and

albumin in growth hormone-stimulated hepatocytes. ProcNatlAcadSci. 1991;88(12):5287–91.

54 Jeejeebhoy KN. Nutrition and serum albumin levels (editorial). Nutrition. 1994;10(4):353.

55 Jorgensen KA, Stoffersen E. Heparin like activity of albumin. Thromb Res. 1979;16(3):569-74.

56 He XM, Carter DC. Atomic structure and chemistry of human serum albumin. Nature. 1992; 358(6383): 209-15.

57 Gosling P. Albumin and the critically ill. Care Crit Ill. 1995;11:57–6

58 Tucker VL, Simanonok KE, Renkin EM. Tissue-specific effects of physiological ANP infusion on blood-tissue albumin transport. American Journal of Physiology. 1992;263(4):R945-53.

59 Parving HH &Gyntelberg F. Transcapillary escape rate of albumin and plasma volume in essential hypertension. Circulation Research. 1973;32(5):643–52.

60 Christensen E, Altman DG, Neuberger J, De Stavola BL, Tygstrup N, Williams R. Updating prognosis in primary biliary cirrhosis using a time-dependent Cox regression model. PBC1 and PBC2 trial groups. Gastroenterology. 1993;105(6):1865-76.

61 Strubelt O, Younes M, Li Y. Protection by albumin against ischaemia- and hypoxia-induced hepatic injury. Pharmacology and Toxicology. 1994;75(3-4):280-4.

62 Dietrich G, Haupt W, Kretschmer V. Disorders of primary hemostasis caused by albumin infusion in hemodilution. BeitragezurInfusionstherapie. 1991;28:331–4.

63 Mulvihill JN, Faradji A, Oberling F, Cazenave JP. Surface passivation by human albumin of plasmapheresis circuits reduces platelet accumulation and thrombus formation. Journal of Biomedical Materials Research. 1990;24(2):155–63.

64 Ramirez-Vick J & Vargas FF. Albumin modulation of paracellular permeability of pig vena caval endothelium shows specificity for pig albumin. American Journal of Physiology. 1993;264(5):H1382–7.

65 Lum H, Siflinger-Birnboim A, Blumenstock F, Malik AB. Serum albumin decreases transendothelial permeability to macromolecules. Microvascular Research. 1991;42(1): 91-102.

66 Zawieja DC. Lymphatic microcirculation. Microcirculation. 1996;3(2):241–3.

67 Qiao RE, Siflinger-Birnboim AL, Lum HA, Tiruppathi CH, Malik AB. Albumin and Ricinuscommunis agglutinin decrease endothelial permeability via interactions with matrix. American Journal of Physiology. 1993;265(2):C439–46.

68 Halliwell B. Albumin-an important extracellular antioxidant?. Biochemical Pharmacology. 1988; 37(4):569-71.

69 De Feo P, Gaisano MG, Haymond MW. Differential effects of insulin deficiency on albumin and fibrinogen synthesis in humans. J Clin Invest. 1991;88(3):833–40.

70 Hoye RC, Bennett SH, Geelhoed GW, Gorschboth C. Fluid volume and albumin kinetics occurring with major surgery. J Am Med Assoc. 1972; 222(10):1255–61.

71 Golub R, Sorrento JJ, Cantu JR, Nierman DM, Moideen A, Stein HD. Efficacy of albumin supplementation in the surgical intensive care unit: a prospective, randomised study. Crit Care Med. 1994; 22(4): 613–9.

72 Glauser MP, Heumann D, Baumgartner JD, Cohen J. Pathogenesis and potential strategies for prevention and treatment of septic shock: an update. Clin Infect Dis. 1994;18:S205–16.

73 Su CH, Tsay SH, Wu CC, Shyr YM, King KL, Lee CH, et al. Factors influencing postoperative morbidity, mortality, and survival after resection for hilarcholangiocarcinoma. Annals of surgery. 1996;223(4):384-94.

74 Finestone HM, Greene-Finestone LS, Wilson ES, Teasell RW. Prolonged length of stay and reduced functional improvement rate in malnourished stroke rehabilitation patients. Arch Phys Med Rehabil. 1996;77(4):340–5.

75 Foley EF, Borlase BC, Dzik WH, Bistrian BR, Benotti PN. Albumin supplementation in the critically ill: a prospective randomised trial. Arch Surg. 1990;125(6):739–42.

76 Chou FF, Sheen Chen SM, Chen YS, Chen MC, Chen FC, Tai DI. Prognostic factors for pyogenic abscess of the liver. Journal of the American College of Surgeons. 1994;179(6):727–32.

77 Knaus WA, Wagner DP, Draper EA, Zimmerman JE, Bergner M, Bastos PG, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalised adults. Chest. 1991:100(6):1619–36.

78 Whicher J & Spence C. When is serum albumin worth measuring? Annals of Clinical Biochemistry. 1987;24(6):572–80.

79 Erstad BL. Serum albumin concentrations: who needs them? Annals of Pharmacotherapy. 1992;26(9):1134–8.

80 Woods MS & Kelley H. Oncotic pressure, albumin and ileus: The effect of albumin replacement on postoperative ileus. The American Surgeon. 1993;59(11):758–63.

81 Kaag MM. Maintenance of adequate serum albumin during extended surgery seems beneficial. Electron Br Med J.1998.

82 Wojtysiak SL, Brown RO, Roberson DO, Powers DA, Kudsk KA. Effect of hypoalbuminaemia and parenteral nutrition on free water excretion and electrolyte-free water resorption. Critical Care Medicine. 1992;20(2):164–9.

83 Stockwell MA, Soni N, Riley B. Colloid solutions in the critically ill. Anaesthesia. 1992;47:3–6.

84 Kurose I, Anderson DC, MiyasakaM,Tamatani T, Paulson JC, Todd RF, et al. Molecular determinants of reperfusion-induced leukocyte

adhesion and vascular protein leakage. Circulation Research. 1994;74(2):336–43.

85 Kan CH, Saffari M, Khoo TH. Prognostic factors of severe traumatic brain injury outcome in children aged 2-16 years at a major neurosurgical referral centre. Malays J Med Sci. 2009;16(4):25–33.

86 Salerno F, Badalamenti S, Lorenzano E, Moser P, Incerti P. Randomized comparative study of hemaccel vs. albumin infusion after total paracentesis in cirrhotic patients with refractory ascites. Hepatology. 1991;13(4):707–13.

87 Rubin H, Carlson S, DeMeo M, Ganger D, Craig RM. Randomized, double-blind study of intravenous human albumin in hypoalbuminemic patients receiving total parenteral nutrition. Critical Care Medicine. 1997;25(2):249–52.

88 McClain C, Cohen D, Phillips R, OttL,Young B. Increased plasma and ventricular fluid interleukin-6 levels in patients with head injury. J Lab Clin Med. 1991;118(3):225-31.

89 Dhandapani SS, Manju D, Vivekanandhan S, Sharma BS, Mahapatra AK. Prognostic value of admission serum albumin levels in patients with head injury. Pan Arab J Neurosurg. 2009;13:60-5.

90 Bernard F, Al-Tamimi YZ, Chatfield D, Lynch AG, Matta BF, Menon DK. Serum albumin level as a predictor of outcome in traumatic brain injury: Potential for treatment. J Trauma. 2008;64(4):872-5.

91 Dziedzic T, Slowik A, Szczudlik A. Serum albumin level as a predictor of ischemic stroke outcome. Stroke. 2004;35(6):e156-8.

92 Pandey MK, Baranwal SK, Panwar DS, Saha SK, Roy K, Ghosh S, et al Serial estimation of serum albumin and its role in traumatic brain injury patients. Asian Journal of Medical Sciences. 2016;(4)7:31-8.

93 Kramer AH, Zygun DA. Neurocritical care: why does it make a difference? CurrOpinCrit Care. 2014;20(2):174–81.

94 Turgeon AF, Lauzier F, Simard JF, Scales DC, Burns KE, MooreL,et al. Mortality associated with withdrawal of life-sustaining therapy for patients with severe traumatic brain injury: a Canadian multicentre cohort study. CMAJ. 2011;183(14):1581–8.

95 VanBeinum A, Hornby L, Ramsay T, Ward R, Shemie SD, Dhanani S. Exploration of withdrawal of life-sustaining therapy in Canadian intensive care units. J Intensive Care Med. 2016;31(4):243–51.

96 Huynh TN, Walling AM, Le TX, Kleerup EC, Liu H, Wenger NS.Factors associated with palliative withdrawal of mechanical ventilation and time to death after withdrawal. J Palliat Med. 2013;16(11):1368–74.

97 Becker KJ, Baxter AB, Cohen WA, Bybee HM, Tirschwell DL, Newell DW, et al. Withdrawal of support in intracerebral hemorrhage may lead to self-fulfilling prophecies. Neurology. 2001;56(6):766–72.

98 Mayer SA, Kossoff SB. Withdrawal of life support in the neurological intensive care unit. Neurology. 1999;52(8):1602–9.

99 O'Callahan JG, Fink C, Pitts LH, Luce JM. Withholding and withdrawing of life support from patients with severe head injury. Crit Care Med. 1995;23(9):1567-75.

100 Muehlschlegel S, Shutter L, Col N, Goldberg R. Decision aids and shared decision-making in neurocritical care: an unmet need in our NeuroICUs. Neurocrit Care. 2015;23(1):127-30.

101 Yap FH, Joynt GM, Buckley TA, Wong EL. Association of serum albumin concentration and mortality Risk in Critically ill patients. AnaesthIntensive Care. 2002;30(2):202-7.

102 McCluskey A, Thomas AN, Bowles BJ and Kishen R. The prognostic value of serial measurements of serum albumin in patients admitted to an intensive care unit. Anaesthesia. 1996;51(8):724-7.

S.no	Cr.no	Name	Age/Sex	Gcs on admission	CT head findings code	MODE OF INJURY	MANAGEMENT	TSP ON ADMISSION	S.ALB D1	S.ALB D3	S.ALB D7	S.ALB D10	ICU STAY DAYS	VENTILATORY SUPPORT DAYS	IONOTROPIC SUPPORT	COMPLICATIONS	DAYS OF HOSPITAL STAY	SURVIVAL /NONSURVIVAL	OUTCOME GOS ON DISCHARGE(F/UF)
1	446653	CM	24 M	<=8	1	RSA	C	6.1	3.65	3.54	3.46	3.31	4	3	N	N	11	S	F
2	455684	S	18	<=8	2	RSA	S	6	3.42	3.2	3.01	2.98	7	6	Y	Y	14	S	UF
3	477307	JS	35	<=8	1	ASSAULT	S	6.1	3.54	3.5	3.46	3.35	5	3	N	N	12	S	F
4	440620	TS	53	<=8	1	RSA	C	6	3.56	3.41	3.4	3.3	5	4	N	N	13	S	F
5	542746	NK	45Fe	<=8	3	RSA	S	6.02	3.52	3.4	3.28	3.01	5	4	N	N	16	S	UF
6	479151	B	22	<=8	2	RSA	S	6.05	3.56	3.3	3.18	3.1	6	4	N	N	14	S	UF
7	510603	JS	38	<=8	5	FALL	C	6	3.58	3.4	3.25	3	7	6	N	Y	16	S	UF
8	469006	NS	62	<=8	1	RSA	S	6	3.4	3.2	3	2.9	8	6	Y	Y	19	NS	UF
9	753477	AS	20	<=8	5	FALL	C	6.2	3.61	3.54	3.42	3.46	6	4	N	N	14	S	F
10	529734	KS	48	<=8	1	FALL	C	5.98	3.53	3.5	3.46	3.38	5	3	Y	N	13	S	F
11	483718	MS	37	<=8	2	RSA	S	6.05	3.54	3.46	3.34	3.25	5	4	Y	N	13	S	UF
12	456054	AS	47	<=8	5	RSA	S	5.8	3.35	3.1	3.05	2.8	8	6	Y	Y	20	S	UF
13	622116	GK	25Fe	<=8	4	FALL	S	5.95	3.36	3.21	3.15	3.1	7	5	N	N	18	S	UF
14	478701	KS	40	<=8	1	RSA	S	5.9	3.43	3.2	3.1	2.8	8	6	Y	Y	20	S	UF
15	473108	AS	26	<=8	2	RSA	S	6.1	3.6	3.53	3.48	3.35	5	4	N	N	13	S	F
16	606840	H	50Fe	<=8	5	RSA	S	5.9	3.4	3.2	3	2.8	9	7	Y	Y	20	NS	UF
17	712353	DS	58	<=8	5	RSA	C	6	3.53	3.46	3.21	3.05	7	5	Y	Y	14	S	UF
18	445405	GK	19Fe	<=8	4	RSA	S	6.05	3.55	3.48	3.4	3.35	3	2	N	N	11	S	F
19	692304	AS	39	<=8	2	RSA	S	6	3.56	3.48	3.34	3.31	5	4	N	N	12	S	F
20	713099	MK	32Fe	<=8	3	RSA	C	6.1	3.6	3.54	3.49	3.4	6	4	N	Y	14	S	F
21	515414	R	29	<=8	2	FALL	S	5.95	3.35	3.21	3.1	3	8	5	Y	N	17	S	UF
22	531791	MK	36	<=8	5	RSA	C	6	3.56	3.34	3.01	2.9	6	4	N	N	18	S	UF
23	480099	NS	30	<=8	5	RSA	S	6	3.4	3.24	3.03	2.81	7	5	N	N	20	NS	UF
24	465562	TS	39	<=8	1	RSA	S	6.08	3.41	3.3	3.21	3.2	6	5	Y	N	12	S	UF
25	537058	RK	23Fe	<=8	5	RSA	C	6.1	3.56	3.45	3.4	3.38	6	4	N	N	13	S	F
26	460845	GD	50	<=8	3	RSA	S	5.98	3.35	3.2	3.05	2.9	7	5	Y	Y	18	NS	UF
27	52019	OK	63	<=8	2	RSA	S	5.9	3.4	3.23	3.15	3.05	6	4	N	N	14	S	UF
28	474803	RS	28	<=8	1	ASSAULT	C	6.1	3.5	3.42	3.3	3.25	5	4	N	N	15	S	UF
29	461852	S	38	<=8	5	RSA	S	5.95	3.5	3.43	3.21	3.05	7	6	N	N	16	S	UF
30	449321	AS	44	<=8	2	RSA	S	6.2	3.64	3.53	3.5	3.45	5	4	N	N	13	S	F
31	455759	MS	25	<=8	5	FALL	C	5.9	3.32	3.3	3.21	3.15	6	4	N	N	16	S	UF
32	589761	GR	49Fe	<=8	1	RSA	S	6.1	3.5	3.46	3.2	3.05	6	5	Y	N	14	S	UF
33	367581	VK	33Fe	<=8	5	ASSAULT	C	6.25	3.56	3.45	3.38	3.3	5	4	N	N	13	S	F
34	702795	AS	20	<=8	2	FALL	S	6	3.41	3.35	3.2	3	6	5	N	N	15	S	UF
35	488460	AK	55Fe	<=8	1	ASSAULT	S	6	3.35	3.2	3.1	2.95	7	6	Y	Y	16	NS	UF
36	468737	R	30	<=8	3	ASSAULT	S	5.95	3.4	3.32	3.2	3.15	6	4	N	N	15	S	UF
37	593310	KK	47	<=8	5	FALL	C	5.9	3.42	3.2	3.05	2.9	4	3	N	N	16	S	UF
38	452922	A	54	<=8	1	RSA	S	6.01	3.46	3.3	3.1	2.85	5	4	N	N	15	S	UF
39	557853	SK	29	<=8	4	RSA	S	5.9	3.46	3.35	3.3	3.2	6	4	Y	N	13	S	UF
40	606148	RS	50	<=8	2	RSA	S	5.85	3.4	3.25	3.1	2.98	7	6	Y	Y	17	S	UF
41	676494	GK	46Fe	<=8	1	FALL	S	5.9	3.2	3.12	3	2.9	8	6	Y	Y	18	NS	UF
42	664544	S	35	<=8	5	FALL	C	6	3.35	3.3	3.12	3.05	6	5	N	N	16	S	UF
43	692192	GS	60	<=8	2	FALL	S	6	3.46	3.32	3.23	3.15	5	3	N	N	15	S	F
44	692319	GS	18	<=8	1	RSA	S	6.02	3.54	3.46	3.31	3.3	4	3	N	N	12	S	F
45	609356	TS	27	<=8	2	FALL	S	6	3.46	3.35	3.26	3.2	5	4	N	N	15	S	UF
46	459395	V	42	<=8	1	RSA	S	5.95	3.45	3.38	3.3	3.25	4	2	N	N	14	S	F
47	629041	TR	19	<=8	2	ASSAULT	C	5.85	3.43	3.3	3.3	3.25	5	4	N	N	15	S	UF
48	545936	G	26	<=8	1	ASSAULT	S	5.8	3.46	3.3	3.15	3	6	4	Y	N	15	S	UF
49	703814	KS	37	<=8	5	RSA	C	5.85	3.4	3.25	3.1	3	7	5	Y	Y	15	NS	UF
50	600265	JK	59Fe	<=8	1	FALL	S	5.8	3.35	3.2	3	2.92	5	4	Y	N	18	S	UF
51	519324	JS	40	<=8	2	ASSAULT	S	5.9	3.4	3.25	3.2	3	6	5	N	N	16	S	UF
52	756144	JK	23Fe	<=8	1	RSA	S	5.95	3.5	3.32	3.15	3	6	4	Y	N	14	S	UF
53	634833	VB	47Fe	<=8	2	ASSAULT	C	6.05	3.56	3.4	3.35	3.3	5	3	N	N	15	S	F
54	576418	SS	34	<=8	4	RSA	S	6	3.5	3.38	3.2	3.18	4	3	N	N	15	S	UF
55	467999	JS	54	<=8	1	RSA	S	6.1	3.65	3.54	3.5	3.46	4	3	N	N	13	S	F
56	387607	K	28	<=8	5	FALL	C	6	3.43	3.31	3.2	3.05	5	4	N	N	18	S	UF
57	582037	NS	35	<=8	2	RSA	C	6.2	3.68	3.5	3.45	3.4	6	5	N	N	14	S	F
58	583770	SR	49	<=8	1	RSA	S	5.85	3.38	3.3	3.1	3	8	6	Y	Y	19	S	UF
59	609845	N	31	<=8	3	FALL	S	6	3.58	3.5	3.46	3.4	4	3	N	N	13	S	F
60	547167	A	18	<=8	5	RSA	C	5.7	3.3	3.2	3.05	3	9	7	Y	Y	20	S	UF
61	476077	K	43	<=8	2	FALL	S	5.9	3.46	3.4	3.35	3.28	6	5	N	N	15	S	F
62	608130	P	30	<=8	1	RSA	S	5.95	3.4	3.25	3.05	2.98	7	6	N	N	16	S	UF
63	367561	VK	32Fe	<=8	5	RSA	C	5.95	3.45	3.35	3.26	3.2	6	5	N	N	15	S	F
64	600265	R	60	<=8	1	RSA	C	5.9	3.35	3.3	3.2	3.15	7	6	N	N	17	S	F
65	704201	MK	40	<=8	1	RSA	C	6.05	3.5	3.35	3.2	3.1	8	5	N	N	16	S	UF
66	543799	BS	55	<=8	1	RSA	S	6	3.4	3.25	3.1	3	10	8	Y	Y	22	NS	UF
67	668760	RS	44	<=8	2	RSA	S	5.9	3.36	3.1	3	2.8	9	8	Y	Y	19	S	UF
68	684461	A	38Fe	<=8	1	RSA	S	5.95	3.4	3.2	3	2.95	11	7	N	Y	20	NS	UF
69	527187	S	23	<=8	4	RSA	S	6.2	3.6	3.54	3.48	3.4	3	2	N	N	10	S	F
70	685859	IS	45	<=8	3	RSA	C	6.15	3.55	3.45	3.4	3.35	4	2	N	N	13	S	F
71	525486	DS	58	<=8	2	ASSAULT	S	6.05	3.45	3.2	3.1	3	7	5	N	N	15	S	UF

S.no	Cr.no	Name	Age/Sex	Gcs on admission	CT head findings code	MODE OF INJURY	MANAGEMENT	TSP ON ADMISSION	S.ALB D1	S.ALB D3	S.ALB D7	S.ALB D10	ICU STAY DAYS	VENTILATORY SUPPORT DAYS	IONOTROPIC SUPPORT	COMPLICATIONS	DAYS OF HOSPITAL STAY	SURVIVAL /NONSURVIVAL	OUTCOME GOS ON DISCHARGE(F/UF)
72	569310	PS	33	<=8	1	FALL	S	6	3.45	3.2	3.2	3.1	7	4	Y	N	16	S	UF
73	603369	NS	49	<=8	1	RSA	C	6.2	3.6	3.4	3.4	3.2	5	4	N	N	12	S	UF
74	576418	SS	32	<=8	2	RSA	S	6	3.46	3.3	3.15	3.05	7	6	Y	Y	17	S	UF
75	632031	R	20Fe	<=8	5	RSA	C	5.8	3.3	3.2	3.05	3	6	4	N	N	18	S	UF
76	529760	G	43	<=8	1	FALL	S	5.95	3.5	3.3	3.05	3	7	5	N	N	16	S	UF
77	703517	DS	38	<=8	1	RSA	S	5.95	3.45	3.25	3.1	3	5	4	N	N	15	S	UF
78	572395	LS	22	<=8	2	RSA	S	6	3.46	3.3	3.15	3	6	4	N	N	14	S	UF
79	645065	S	64	<=8	5	RSA	C	6	3.55	3.45	3.4	3.35	7	4	N	N	15	S	F
80	608113	RS	50	<=8	1	RSA	S	5.85	3.35	3.2	3	2.9	7	6	Y	N	16	S	UF
81	615522	BS	35	<=8	5	RSA	C	6.05	3.5	3.45	3.4	3.4	6	4	Y	Y	16	S	F
82	739537	N	46Fe	<=8	1	RSA	S	6	3.4	3.21	3.2	3	8	6	N	Y	18	NS	UF
83	713914	MK	30Fe	<=8	2	RSA	S	5.95	3.45	3.3	3.3	3.25	6	3	N	N	14	S	F
84	647775	S	24	<=8	5	RSA	C	6	3.56	3.5	3.4	3.4	6	4	N	N	14	S	F
85	649104	BS	56	<=8	2	RSA	C	6	3.6	3.5	3.45	3.3	6	5	Y	N	17	S	F
86	650562	A	31	<=8	5	RSA	S	5.95	3.5	3.4	3.2	3.1	8	6	Y	Y	18	S	UF
87	628226	R	19	<=8	2	RSA	C	5.9	3.45	3.4	3.35	3.3	5	3	N	N	18	S	F
88	154287	T	35Fe	<=8	3	RSA	S	5.85	3.36	3.2	3.05	2.98	8	7	Y	Y	18	NS	UF
89	640952	NS	60	<=8	1	FALL	S	5.88	3.35	3.1	3.1	2.9	9	6	N	Y	24	S	UF
90	681541	PK	42Fe	<=8	1	ASSAULT	S	6	3.4	3.3	3.05	3	6	4	N	N	20	S	UF
91	572395	GS	22	<=8	4	FALL	S	5.9	3.45	3.3	3.25	3.2	4	3	N	N	10	S	UF
92	634692	IS	37	<=8	5	RSA	C	5.95	3.4	3.4	3.1	3	8	5	Y	N	18	S	UF
93	641095	AS	46	<=8	2	RSA	C	6.02	3.54	3.4	3.25	3.1	7	4	N	N	16	S	UF
94	624170	AG	55	<=8	1	RSA	S	5.8	3.3	3.2	3.15	3	8	5	Y	N	18	S	UF
95	743859	BJ	33Fe	<=8	5	RSA	C	6	3.46	3.4	3.32	3.3	7	6	N	Y	17	S	UF
96	746523	RS	24	<=8	2	RSA	C	5.9	3.4	3.35	3.3	3.3	6	4	N	N	16	S	UF
97	745871	MK	47	<=8	1	FALL	S	5.8	3.32	3.2	3.2	3	9	8	Y	Y	20	S	UF
98	756601	HR	59	<=8	2	RSA	S	5.7	3.2	3.05	3.05	2.85	10	8	Y	Y	21	S	UF
99	748214	K	28Fe	<=8	1	RSA	S	6	3.3	3.15	3.15	2.9	9	7	Y	Y	18	S	UF
100	558975	SS	44	<=8	2	RSA	S	6	3.4	3.36	3.3	3.1	6	5	Y	N	16	S	UF
101	601721	AK	25Fe	<=8	5	RSA	C	6.05	3.46	3.42	3.4	3.25	8	6	Y	Y	21	NS	UF
102	576900	IS	49	<=8	5	RSA	C	5.9	3.45	3.3	3.3	3	7	5	N	N	17	S	UF
103	587500	JS	34	<=8	5	RSA	C	5.95	3.46	3.36	3.35	3.05	7	6	Y	N	16	S	UF
104	460984	RS	55	<=8	1	FALL	S	5.8	3.34	3.2	3.25	2.95	9	7	Y	Y	18	NS	UF
105	510661	BS	41	<=8	3	RSA	S	6	3.5	3.4	3.45	3.1	7	6	Y	Y	16	S	UF
106	573386	HS	18	<=8	2	FALL	S	5.95	3.35	3.3	3.2	3.155	7	4	N	NN	14	S	UF
107	474906	SK	37Fe	<=8	5	RSA	S	6	3.4	3.27	3.25	3.15	8	5	N	N	19	S	UF
108	601721	R	26	<=8	5	FALL	S	6.05	3.4	3.4	3.27	3.2	6	4	N	N	17	S	F
109	570416	U	63Fe	<=8	1	RSA	C	6.1	3.56	3.5	3.43	3.3	7	4	Y	Y	15	S	F
110	758095	RK	34	<=8	5	RSA	S	6.05	3.35	3.3	3.15	3.05	10	7	N	Y	23	S	UF

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Date 18/5/2020

The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.05.2019 has approved the plan of thesis of **Dr. Vikram Chaudhary**, a student of your college for **Mch Neuro Surgery** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

Role of serum albumin as a prognostic marker of outcome in patients with severe traumatic brain injury.

Supervisor
Dr. Ashwani K chaudhary, Prof
Dept of Neuro-surgery, DMCH,
Ludhiana

Co-Supervisor

Dr. R.K Kaushal
Prof & Head Dept of Neuro
surgery DMCH, Ludhina

The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

S P Singh

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

ROLE OF SERUM ALBUMIN AS A PROGNOSTIC MARKER OF OUTCOME IN PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED
IN PARTIAL FULFILMENT OF THE REQUIREMENTS
FOR THE DEGREE OF

M.Ch.
In
NEUROSURGERY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES
FARIDKOT

FEBRUARY, 2018

DR. VIKRAM CHAUDHARY

DEPARTMENT OF NEUROSURGERY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	**Role of serum albumin as a prognostic marker of outcome in patients with severe traumatic brain injury**
For the degree of	**M.Ch. Neurosurgery**
Name of the candidate	**Dr. VikramChaudhary**
Supervisor	**Dr. Ashwani K Chaudhary,** Professor, Department of Neurosurgery, DMCH, Ludhiana
Co-supervisor	**Dr. R.K. Kaushal,** Professor and Head, Department of Neurosurgery, DMCH, Ludhiana
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

INTRODUCTION

Head injury remains one of the commonest causes of morbidity and mortality to the mankind. The accurate prediction of outcome of patients with severe traumatic brain injury is still not possible despite intensive ongoing research.

AIMS & OBJECTIVES

The present study aims to prognosticate the outcome of patients with severe traumatic brain injury according to the serrum albumin at the time of admission.

MATERIAL & METHODS

Present study will be conducted in patients admitted with severe traumatic brain injury in the casuality and departmentof neurosurgery of dayandand medical college and hospital ludhiana

CLINICAL SIGNIFICANCE

Our study has aims to establish a relationship between the patients level of serrum albumin at time of admission with the outcome of patient at discharge

KEYWORDS

Serrum, Albumine, Brain

Candidate's sign **Co- supervisor's sign** **Supervisor's sign** **Principal's sign**

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"ROLE OF SERUM ALBUMIN AS A PROGNOSTIC MARKER OF OUTCOME IN PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY"** exist in the Department of Neurosurgery, Dayanand Medical College, Ludhiana& will be provided to the candidate. We will see that the data being included in the thesis are genuine & is collected by the candidate himself under our supervision & guidance.

Supervisor

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Date:

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	**Dr. Vikram Chaudhary**
Department	**Neurosurgery**
Topic of Thesis	**Role of serum albumin as a prognostic marker of outcome in patients with severe traumatic brain injury**
Likely date of appearing in PG examination	May 2020
Date of enrollment	14th September 2017
Name of Head of Department	Dr. R.K. Kaushal
1) Supervisor **2) Co-Supervisor**	Dr. Ashwani K Chaudhary Dr. R.K. Kaushal
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
1. HOD Pharmacology	1. HOD Physiology
2. HOD Surgery	2. HOD Pathology
3. HOD Pathology	3. HOD Pharmacology
4. HOD Medicine	4. HOD SPM
5. Dean Academics	5. HOD Medicine
6. Vice Principal	6. HOD Surgery
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Research Committee

Approved: Yes / No

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Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

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2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA
3	COURSE OF STUDY AND SUBJECT	M.CH. NEUROSURGERY
4	DATE OF ADMISSION OF COURSE	14TH SEPTEMBER 2017
5	TITLE OF THE TOPIC	ROLE OF SERUM ALBUMIN AS A PROGNOSTIC MARKER OF OUTCOME IN PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY.

6 BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

The uncertainty that exists about the likely outcome after traumatic brain injury (TBI) is encapsulated in the Hippocratic aphorism: "No head injury is so serious that it should be despaired of nor so trivial that it can be ignored." Today, physicians' estimates of prognosis are still often unduly optimistic, unnecessarily pessimistic, or inappropriately ambiguous.[1] It still remains impossible to say with certainty what will be the future course of events in an individual patient, but intensive research in the last two decades has made it possible to be much more confident about what is likely to happen, and to consider prognosis in terms of probabilities rather than prophecies.[2]

In Asian countries the rapid urbanization has increased the risk of TBI.[3] India remains in the leading position in the world in fatalities due to road accidents.[4] Even if people survive, the concomitant physical disabilities, long-term cognitive and psychological damage pose a major threat. With the subsequent secondary damage setting insidiously, the pathological sequelae warrant a multidisciplinary approach for management and longer period of stay in the ICU setting. It takes a heavy toll on both financial status of the patients and the hospital's available resources. In order to mitigate the misery of the patients and to judiciously allocate the hospital resources, it becomes mandate to predict the favourable outcome earlier in order to take decision whether to continue aggressive therapeutic measures or not.[5] This will guide the clinicians immensely in deciding the mode of patient management. But predicting the prognosis of TBI remains a challenge for clinicians. Early

intensive rehabilitation increases the survival rate and helps in restoration of functional capacity of the patients.[6]

Prediction of outcome involves making probability statements that depend on a logical relationship between outcome and features encapsulated in antecedent, early data. The advances in prognosis reflect the establishment of methods for categorizing outcome[7] and early injury severity.[8] Although clinicians usually attempt to take a wide range of factors into account when making clinical decisions and assessing prognosis, there is probably a redundancy in this effort to be complete. In practice, relatively few features have been found to contain most of the prognostic information.[2] These include the patient age, clinical indices indicating the severity of brain injury (e.g., the depth and duration of coma and other neurological abnormalities), and the results of investigation and imaging studies, particularly intracranial pressure (ICP) and computed tomography (CT) scanning, which disclose the nature of brain injury and its effects on intracranial dynamics. Even though there is little doubt regarding the importance of these features from clinical experience, there are still debates about the precise nature of their relationships and about exactly how the different features should be assessed, categorized, and—most importantly—utilized.[2]

Traumatic brain injury (TBI) is a heterogeneous disorder characterized by acute brain injury resulting from external mechanical forces exerted on the head. In clinical settings, the Glasgow Coma Scale (GCS) is commonly used to stratify the severity of TBI, where mild TBI (mTBI), moderate TBI and severe (sTBI) constitute a GCS score of 13-15, 9-12 and 3-8 respectively.[9]

Assessment of TBI

There are different systems available to evaluate the extent of brain injury. Neuro-psychological examination like Glasgow Coma Scale (GCS) and pupil response are widely used for the assessment of the severity of brain injury.[10] The neuroimaging techniques, such as computed tomographic scanning (CT scan) and magnetic resonance imaging (MRI) have emerged as the choice of investigation. But all these have limitations such as poor sensitivity and failure to detect secondary pathological events.[11] Hence exhaustive research has been carried out for identifying better prognostic marker, preferably a serum bio marker. These efforts to identify an ideal biomarker which could reflect the pathology of TBI and secondary injury have yielded meagre success. This is evident from the finding that the markers released from the brain cells are also elevated in non- brain pathological conditions and are non-specific.[12]

Behavior	Response	Score
Eye Opening Response		
	Spontaneously	4
	To speech	3
	To pain	2
	No response	1
Best Verbal Response	Oriented to time, place, and person	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No response	1

Best Motor Response	Obeys commands	6
	Moves to localized pain	5
	Flexion withdrawal from pain	4
	Abnormal flexion (decorticate)	3
	Abnormal extension (decerebrate)	2
	No response	1

Total Score: 15

Comatose: 8 points or less

Totally unresponsive: 3 points

Mild brain injury = 13-15 points; **Moderate Brain Injury** = 9-12 points;

Severe Brain Injury = 3-8 points

Pathophysiology of TBI

The neurobiological changes following TBI are complex and not fully understood. Some layers of complexity arise from unique anatomical features such as the elongated shape of a neuron, the skull that both protects the brain and constitutes a harmful closed compartment in the case of intracranial volume expansion, the cerebrospinal fluid and blood-brain barrier (BBB), which both maintain and perpetuate the unique intracerebral environment.

The BBB is highly selective and plays an important role in allowing proteins or biomarkers entering the blood stream. In the acute phase of TBI, the disruption of the BBB may cause vasogenic or cytotoxic brain edema, leading to the expansion of brain volume, which in turn increases intracranial pressure (ICP), impairs cerebral perfusion and subsequently causes ischemic injury.[9]

Structural injuries to the brain can be categorized into focal and diffuse. Focal injuries are usually associated with higher energy trauma and include cortical

or subcortical contusions and lacerations as well as intra cerebral hemorrhage.[9]

Biomarkers for TBI

Biomarkers are molecules that can be measured in accessible biological fluids, that reflect physiological, pharmacological, or disease processes and can suggest the etiology of, susceptibility to, activity levels of, or progress of a disease. Biomarkers may be classified into at least four categories: diagnostic, prognostic, predictive, and pharmacodynamic. Diagnostic biomarkers are markers that reliably identify a certain disease with clinically meaningful sensitivity and specificity. Prognostic biomarkers are baseline measurements that categorize patients by degree of risk for disease progression and inform about the natural history of the disorder. Predictive biomarkers are baseline characteristics that categorize patients by their likelihood of response to a particular treatment. Finally, pharmacodynamic (or theragnostic) biomarkers are dynamic measurements that show that a biological response has occurred in a patient after a therapeutic intervention.

The search for biomarkers in CSF for the management of neurological disorders has been an intense area of research for decades. Owing to the close proximity of CSF to the brain parenchyma, CSF is considered as a suitable biofluid to monitor pathophysiological changes affecting the brain. CSF biomarkers such as white blood cell counts and CSF/blood glucose ratio as well as intrathecal IgG production have primarily been used to identify or rule out CNS infection and inflammation for decades.[9]

In recent decades, advances in assay development have enabled researchers to measure biomarkers believed to reflect many aspects of brain pathology,

such as axonal (T-tau, NFL, SNTF), amyloid (Aβ) and astroglial pathology (S100B, GFAP). In the context of TBI, increased levels of T-tau and NFL measured in CSF have also been found in athletes and patients with traumatic brain injury. Increased levels of GFAP and S100B measured in CSF have also been reported in individuals with traumatic brain injury CSF is often obtained through lumbar puncture, which may not always be practical to perform on routine clinical basis. Blood-based biomarkers for neuronal injury have been evaluated in few studies of patients with AD and TBI.[9]

Role of serum albumin as biomarker of TBI

Acute Inflammation following the primary injury remains central to the pathogenesis of secondary injury that influences the outcome of the patients.[11] A repertoire of inflammatory molecules are pressed into service, the key player being cytokines as part of local and systemic acute phase response. Few studies explored the utility of using the circulating inflammatory mediators as the predictors of outcome in injury.[15] The acute inflammatory response, designed to be protective mechanisms, can override at times, leading to unfavourable outcome. Considerable attention has been directed towards the utility of acute phase reactants as prognostic marker for predicting outcome. Among the acute phase reactants albumin is ideally a candidate for research as the measurement is easily available and routinely done.[6]

Albumin (69Kda) is the major protein of the human plasma accounting to about 60% of the total plasma protein.[10] Albumin is produced by the liver at a rate of 9 to 12 g/day. Its hepatic synthesis is primarily affected by osmotic colloid pressure and inflammatory states, but also, and to a lesser degree, by

nutritional status and hormones. It is one of the negative acute phase reactants and its level tend to fall in the plasma as a result of injury or infection independent of the nutritional status.[16] Many studies had highlighted the role of albumin as a prognostic marker in life threatening illnesses, various types of cancer such as colorectal, lung and breast cancer.[6] It has also been studied to determine the clinical outcome following cardiac surgery.[17] Du Chen, Long Ba, et al, have studied the use of serum albumin along with pre-albumin to predict the poor outcome in TBI and observed serum albumin serve as a better marker.[18]

Serum albumin is a widely used method of accessing nutritional and inflammation status in both acute and chronically ill patients. Al-though many studies explored the relationship between serum albumin levels and the duration of weaning in patients with mechanical ventilation, but its effect on patients' outcome of wean-ing was still unknown. The aim of this study was to find the relationship between serum albumin and duration of weaning in patients with isolated TBI.[19]

Assessing the outcome of TBI

Death or severe disability is common after sTBI. Outcome or recovery in these patients can be assessed using the Glasgow Outcome Scale (GOS). GOS is a broad functional outcome scale, taking into account whether the patient depends upon others for daily support due to mental or physical disability and whether major or minor neurological or psychological disabilities beyond that are present or not. Patients are categorized into one of five recovery categories: death, vegetative state, severe disability, moderate and good recovery. Analysis of data on a large amount of patients with moderate

to sTBI have revealed that age, papillary diameter and light reflex, GCS motor score and CT findings are good predictors of GOS score.[9]

Glasgow Outcome Scale (GOS)

Score	Term	Definition
1	Dead	No life
2	Vegetative state	Unaware of self and environment
3	Severe disability	Unable to live independently
4	Moderate disability	Able to live independently
5	Mild disability	Able to return to work/school

6.2 REVIEW OF LITERATURE

Severe Traumatic Brain Injury (TBI) is a major cause of disability and death in the young. Severe TBI initiates a complex cascade of metabolic perturbations with the primary injury triggering secondary events that evolve over many days, leading to deleterious pathophysiological and biochemical reactions. Numerous studies have consistently demonstrated increased protein catabolism following TBI. Surprisingly, only a few biochemical markers have been identified to prognosticate the patients' response to brain injury. These markers also exhibit changes over time in patients of trauma as a component of metabolic response to injury or infection (MRII), independent of the nutritional status.[20]

SS Dhandapani et al 2010 studied biochemical changes in patients with severe traumatic brain injury, with respect to neurological outcome. Adult patients admitted within 24 hours of traumatic brain injury with Glasgow Coma Score 4-8, were prospectively studied for changes in various biochemical parameters. Outcome was assessed at 6 months. The mean serum albumin levels showed progressive fall till 2 weeks from 3.23 g/dL to nadir value of 2.86 g/dL, followed by mild increase to 2.99 g/dL at 3 weeks ($p<0.001$). The mean daily urine creatinine values demonstrated significant fall from 1255.4 mg/d to 1010.2 mg/d at 3 weeks ($p<0.001$). There was significant increase in mortality at 2 months among patients with atleast 15% fall in serum albumin and urine creatinine less than 1000 mg/d at 3 weeks ($p < 0.005$). Unfavorable outcome was noted in 12 out of 15, with at least 15% fall in serum albumin at 3 weeks, compared to 11 out of 25, with less than 15% fall in serum albumin ($p=0.03$). Unfavorable outcome was also noted in 16 out of 22, with low urine

creatinine (<1000 mg/d) at 3 weeks, compared to 6 out of 17, with normal urine creatinine (p=0.02). In patients with severe TBI, unfavorable neurological outcome at 6 months was associated with 15% fall of serum albumin or low urinary creatinine at 3 weeks, more so with the former.[20]

Du Chen et al. studied 326 patients of TBIThey were divided into a favorable group (GOS: 3 to 5) and an unfavorable group (GOS: 1 to 2). Serum albumin and prealbumin were measured from vein blood within 24 h after admission. Ninety one (27.9%) patients were with poor outcome (GOS: 1 to 2). The unfavorable group had lower albumin and prealbumin (P,0.001). Albumin and prealbumin were both positively correlated with GCS (r = 0.489, P,0.001; r = 0.222, P, 0.001, respectively) and GOS (r = 0.518, P,0.001; r = 0.314, P,0.001, respectively). After adjustment for confounding factors, the odds ratios of albumin and prealbumin were 0.866, 95% CI: 0.829 to 0.904 and 0.990, 95% CI: 0.985 to 0.995, respectively. In subgroup of GCS#8 (n = 101), the crude and adjusted odds ratios of serum albumin were both statistically significant (P = 0.027, P = 0.033, respectively), while prealbumin were not (P = 0.553, P = 0.576, respectively). The study concluded that both serum albumin and prealbumin may be used as predictors for unfavorable outcome of TBI, but the performances are significantly different, and former is much better. Especially, in patients of severe TBI (GCS#8), serum albumin is determined as an independent predictor, while prealbumin seems to be with no predictive value.[21]

Zhi-Yong Zhao et al 2016 studied Serum albumin as a predictor for duration of weaning in patients with traumatic brain injury. A retrospective study was conducted in the ICU of Huashan Hospital affiliated to Fudan University

between January 2009 and June 2014. 104 patients suffering from traumatic brain injury were included. Serum albumin concentration, Motor GCS score and other clinical and laboratory data were collected and analyzed. Serum albumin concentration was associated with duration of weaning, patients with higher albumin levels had shorter duration of weaning, either at admission ($P = 0.002$) or at weaning ($P < 0.001$). Lower albumin levels appeared to be more frequent in patients with epidural hematoma ($P = 0.004$). Serum albumin level seems to be an independent predictor for duration of weaning in patients with isolated traumatic brain injury. Therefore it is advisable that albumin can be used for clinical instruction for weaning in patients with isolated brain injury.[22]

Mithilesh Kumar Pandey et al 2016 studied serial estimation of serum albumin and its role in traumatic brain injury patients In the study 86 (43%) patients having hypoalbuminemia (< 3.5 gm/dl) and falling trend in admission serum albumin levels from day 1 to 10th day with decrement in GCS was statistically highly significant ($p < 0.001$) as hypoalbuminemia was noted in 68%, 39.65 and 33.43% patients with severe, moderate and mild head injury respectively. The present study was showed that female TBI patients having less no. of hypoalbuminemia compare to male as 77.7%, 45.4%, 31.4% male and 42.8%, 28.5%, 27.2% female having hypoalbuminemia (< 3.5 gm/dl) in severe, moderate and mild head injury respectively and statistically significant difference in severe and moderate group.[23]

SivaaRajendran et al 2017 Evaluated role of serum albumin as a prognostic marker in traumatic brain injury. Fifty four consecutive patients admitted to emergency intensive care with varying degrees of head injuries, were grouped

into 3 categories based on the admission time Glasgow Coma Scale (GCS) as mild (13 to 15), moderate (9-12), and severe brain injury(8 or less) and their serum albumin were estimated. Out of 54 patients, 15 had hypoalbuminemia (albumin <3.5g/dL), while for the rest the levels were normal. In the normal albumin group 87% patients showed good outcome and only 13% showed poor outcome. With Kaplan-Meier survival curves, patients with normal albumin levels showed a significantly higher chance to survive than patients with hypoalbuminemia. Further stratification of our cohort into groups according to the interquartile range of serum albumin and comparing it with their clinical outcome by Cox regression indicated that the probability of mortality increased with the decrease in serum albumin (hazard ratio[HR] = 0.15; 95% CI = 0.03- 0.6) with a significant p value of <0.05.[6]

6.3 AIMS AND OBJECTIVES OF THE STUDY

To study the role of serum albumin as a marker for predicting prognosis in patients admitted with severe head injury defined as having Glasgow coma score of less than 8.

7.0 MATERIALS AND METHODS

7.1 SOURCE OF DATA

Patients admitted to DMCH during the period of Feb 2018 to July 2019 with severe traumatic brain injury having Glasgow coma score of less than 8 will be included in the study.

7.2 METHODS OF COLLECTION OF DATA

All the patients will be evaluated neurologically and radiologically with non contrast CT of head. On admission the serum albumin of the patient will be noted, appropriate management plan will be decided based on examination and CT findings. Patients will be managed in neurointensive care unit and neurosurgery ward with appropriate ventilator and ionotropic support as required.

Patient will undergo serial assessment of their serum albumin at the day 1 (on admission) day 3 day 7 and day 10 of the stay irrespective of patient undergoing surgical or non surgical management.

The outcome of the patient will be assessed according to Glasgow outcome score at the time of discharge. Patients will be divided into two groups, group A unfavourable (GOS grades-2,3) and group B favourable (GOS grades 4,5), the mean value of serum albumin will be correlated to the outcome of the patients at discharge. The value of serum on admission will be correlated with duration of stay in hospital, duration of ventilator support required, need for ionotropic support.

Inclusion criterion

1. Patients admitted with severe head injury GCS 8 or less
2. Head injury verified on CT or MRI

Exclusion criterion

1. Patients less than 12 years and more than 60 years
2. Polytrauma patients
3. Patients with hepatic disease, chronic renal failure and cardio-respiratory disease

Duration of study

Study will be conducted from Feb 2018 to july 2019 on the patients admitted with severe traumatic brain injury

Statistical Analysis

Appropriate statistical methodsand tests will be applied.

Management plan

Patients will be managed according to the examination and radiological findings and appropriate management plan will be decided whether surgical or non surgical. Icu care and ventilator and ionotropic support will be given as required

Outcome

Outcome will be assessed at the end of hospital stay by Glasgow outcome score, duration of stay, need for ventilator support, ionotropic support and complications will be analysed

Glasgow Outcome Scale (GOS)

Score	Term	Definition
1	Dead	No life
2	Vegetative state	Unaware of self and environment
3	Severe disability	Unable to live independently
4	Moderate disability	Able to live independently
5	Mild disability	Able to return to work/school

7.3 INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS

All routine investigations

Serum albumin on admission and at 3rd, 7th, and 10th day

CT head

MRI brain

Surgery as according to the injury

7.4 ETHICAL CLEARENCE BEEN OBTAINED FROM YOUR INSTITUTION

Attached Herewith

8. LIST OF REFERENCES

1. Barlow P, Teasdale G. Prediction of outcome and the management of severe head injuries: the attitudes of neurosurgeons. Neurosurg.1986;19:989-991.
2. ChesnutRM, Ghajar J, Maas AIR, Marion DW, Servadei F, Teasdale GM. Early indicators of prognosis in severe traumatic brain injury. Available at url: https://www.braintrauma.org/uploads/01/03/prognosis_guidelines.pdf
3. Shekhar C, Gupta LN, Premsagar IC, Sinha M, Kishore J. An epidemiological study of traumatic brain injury cases in a trauma centre of New Delhi (India). J Emerg Trauma Shock. 2015;8(3):131–9.
4. Puvanachandra P, Hyder AA. The burden of traumatic brain injury in Asia: A call for Research. Pak J Neurol Sci. 2009;4:27–32.
5. Finfer SR, Cohen J. Severe traumatic brain injury. Resuscitation. 2001;48(1):77-90.
6. Rajendran S, Govindan T, Vedavyasan M, Selvaraj K. Evaluation of serum albumin as a prognostic marker in traumatic brain injury. International Journal of Clinical Biochemistry and Research. 2017;4(3):299-304
7. Jennett B, Bono M. Assessment of outcome after severe brain damage. A practical scale. Lancet. 1975;1:480-4.
8. Teasdale G, Jennet B. Assessment of coma and impaired consciousness. Lancet.1974;2:81-4.
9. Pashtun Shahim Blood Biomarkers for Traumatic Brain Injury http://hdl.handle.net/2077/39572

10. Turgeon AF, Lauzier F, Zarychanski R, Fergusson DA, Léger C, McIntyre LA, et al. TBI-Prognosis Study Team and the Canadian Critical Care Trials Group. Prognostication in critically ill patients with severe traumatic brain injury: the TBI-Prognosis multicentre feasibility study. BMJ Open. 2017;7(4):e013779.

11. Papa L, Ramia MM, Edwards D, Johnson BD, Slobounov SM. Systematic review of clinical studies examining biomarkers of brain Injury in athletes after sports-related concussion. Journal of Neurotrauma. 2015;32:661–73.

12. Arsalan S. Haqqani, James S. Hutchison, Roxanne Ward, Danica B. Stanimirovic, For The Canadian Critical Care Translational Biology Group. Protein Biomarkers in Serum of pediatric patients with SevereTraumatic Brain Injury Identified by ICAT–LC-MS/MS. Journal of Neurotrauma. 2007;24(1):54–74.

13. Adams JH, Doyle D, Ford I, Gennarelli TA, Graham DI, McLellan DR. Diffuse axonal injury in head injury: definition, diagnosis and grading. Histopathology. 1989.15(1):49-59.

14. Johnson VE, StewartW, SmithDH. Axonal pathology in traumatic brain injury. Exp Neurol. 2013;246:35-43.

15. Adrian H, Marten K, Salla N, Lasse V. Biomarkers of Traumatic Brain Injury: Temporal Changes in Body Fluids. eNeuro. 2016;3(6):ENEURO.0294-16.2016.

16. Burtis CA, Ashwood ER, Bruns DE. Teitz text book of clinical chemistry and molecular diagnosis. 4th ed. New Delhi: Elsevier Saunders; p. 546.

17. KoertzenM, PunjabiPP, LockwoodGG. Pre-operative serum albumin concentration as a predictor of mortality and morbidity following cardiac surgery. Perfusion. 2013;28(5):390–4.

18. Chen D, Bao L, Lu SQ, Xu F. Serum albumin and prealbumin predict the poor outcome of traumatic brain injury. PLoS One. 2014;9(3):e93167.

19. Zhao Z-Y, Wu N, Deng SC, Zhou Y, Cao T-W. Serum albumin is a predictor for duration of weaning in patients with traumatic brain injury. Int J ClinExp Med. 2016;9(2):4041-6.

20. Dhandapani SS, Manju D, Vivekanandhan S, Agarwal M, Mahapatra AK et.al Prospective longitudinal study of biochemical changes in critically ill patients with severe traumatic brain injury: Factors associated and outcome at 6 months Indian Journal of Neurotrauma. 2010;7:23-8.

21. Chen D, Bao L, Lu SQ, Xu F. Serum Albumin and Prealbumin Predict the Poor Outcome of Traumatic Brain Injury. PLoS One. 2014;9(3):e93167.

22. Pandey MK, Baranwal SK, Panwar DS, Saha SK, Roy K, Ghosh S, et al Serial estimation of serum albumin and its role in traumatic brain injury patients. Asian Journal of Medical Sciences. 2016;7:31-8.

PROFORMA

S.No. __

Name	Age	Sex
Address	Ph. No.	
CR No		
DOA	DOD	DOS

EXAMINATION

GCS at admission

Pupils

PR

BP

INVESTIGATIONS

NCCT HEAD

MRI BRAIN

Blood investigations

HB

TLC

PLATELETS

PT /INR

S.CREATININE

SERRUM LFT

Signature of Candidate **Signature of Supervisor**

ECG

TOTAL SERRUM PROTEINS

SERRUM ALBUMINE AT TIME OF ADMISSION

SERIAL ESTIMATION OF SERRUM ALBUMINE

DAY	SERRUM ALBUMINE
1(admission)	
3	
7	
10	

Days of ICU Stay

Days of ventilator support

Need for ionotropic support (yes / no)

Type of management (surgical/ non surgical)

If surgical type of surgery

Outcome of the patient at discharge- Glasgow outcome score

NON FAVOURABLE- GOS grade 2,3

FAVOURABLE- GOS grade 4,5

Complications

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....

am willing to participate in the study **"ROLE OF SERUM ALBUMIN AS A PROGNOSTIC MARKER OF OUTCOME IN PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out of the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____ निवासी _____ इस शोधकार्य "**ROLE OF SERUM ALBUMIN AS A PROGNOSTIC MARKER OF OUTCOME IN PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY**" में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫ਼ਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____ **"ROLE OF SERUM ALBUMIN AS A PROGNOSTIC MARKER OF OUTCOME IN PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY"** ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ